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ALTERATION IN P-R INTERVAL ASSOCIATED WITH CHANGE IN POSTURE

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R.C.A.F.

INTRODUCTION

IN THE past five to six years, the recording of many thousands of electrocardiograms in healthy normal men for the purpose of aircrew or other military medical examinations has brought to light many interesting examples of "so-called" electrocardiographic abnormalities in healthy normal men without any apparent evidence of heart disease.

During a study of the routine electrocardiograms of Royal Canadian Air Force aircrew in 1940-1941 four cases were discovered which showed significant alteration in the P-R interval with change in posture. In one of these the reduction in the P-R interval was very marked, from 0.40 second to 0.20 second on changing from the recumbent to the upright position.

It has been shown by several workers that alterations in the direction and amplitude of the wave complexes are sometimes associated with changes in posture and respiration.[1, 3, 5, 6, 8, 9] Changes have also been reported in the P-R interval and other time relationships in association with heart disease and with various physiologic factors.[4, 11]

A case of persistent functional heart block apparently due to vagal influence has been reported by Poel.[7] In this case a change in posture from lying to standing position changed the P-R duration from 0.36 second (standing) to 0.30 second (sitting). Poel also reviews three other cases of incomplete heart block due to vagal effect. The effect of posture, however, was not determined. Case 4 of the present report is of particular interest in that incomplete heart block is present in the recumbent position and abolished in the sitting or standing position. It differs from Poel's case in that the P-R duration comes within the accepted limit of P-R duration and therefore is not a case of persistent A-V block. The mechanism, however, is most likely due to a vagal effect as discussed in Poel's report.

MATERIAL AND METHODS

Routine electrocardiograms were taken on R.C.A.F. aircrew trainees in 1940 and early 1941. The men were between the ages of 18 and 32 years, the majority between the ages of 18 and 26 years. All had passed the standard R.C.A.F. medical examination at a Recruit-

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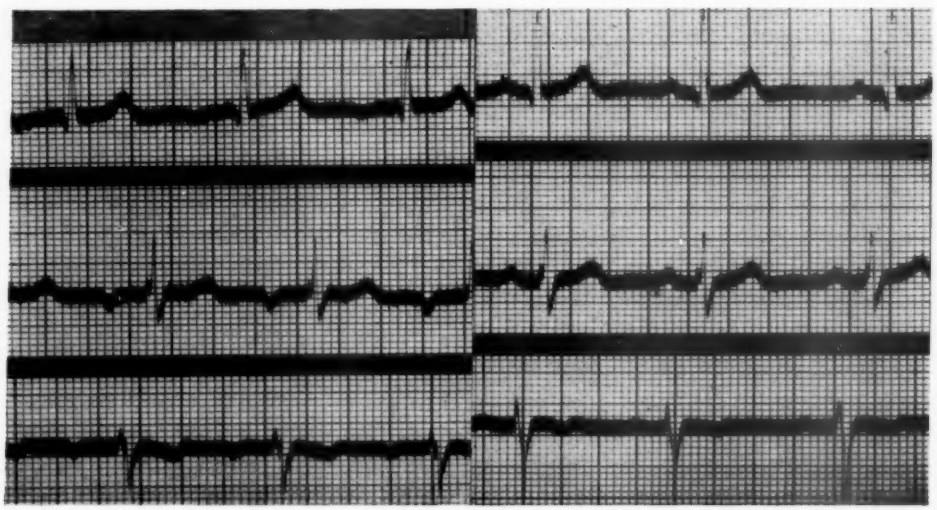
ing Center. A complete clinical recheck was made, one or two months later, by a Medical Selection Board, and at that time the electrocardiograms were recorded.

The routine electrocardiograms were taken with a portable Cambridge (English) electrocardiograph which recorded the three standard leads on a single film. The deflection of the galvanometer string was standardized before each lead was recorded. All the records were taken in the recumbent position.

As mentioned in previous reports,[2, 8] a considerable number of abnormal electrocardiographic findings were noted, including 2.2 per cent of records with a P-R interval greater than 0.20 second.

One group of twenty men whose original electrocardiograms had shown a prolonged P-R interval were recalled for further investigation, including the effect of changes in posture and respiration on the electrocardiogram. The first record of this special study was also taken in the recumbent position. It was compared with the previous one and served as a check on the recording technique. It was also used as a basis for comparison of further records, taken immediately afterward in different postures and phases of respiration.



A. *B.*

Fig. 1.—*A*, Case 3. Recumbent; prolonged P-R interval; negative P waves. *B*, Case 3. Sitting, normal P-R interval; positive P waves.

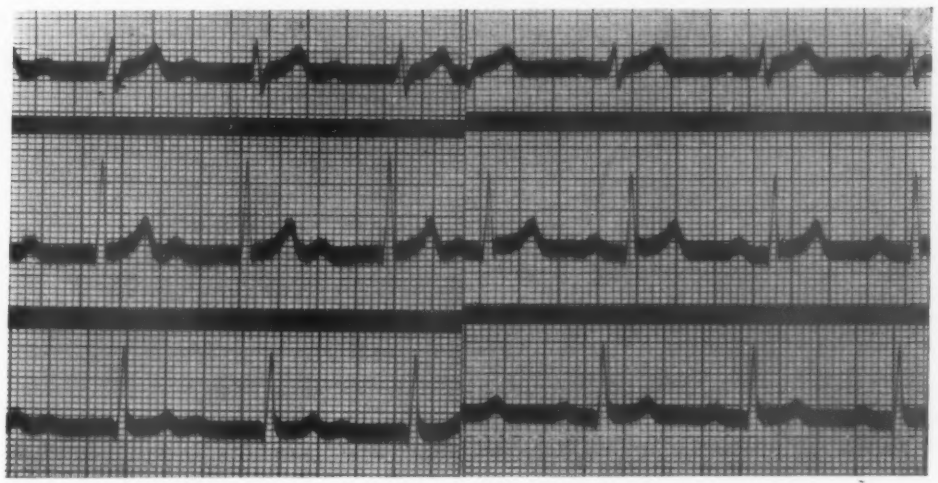
OBSERVATIONS

A. *Decrease in Prolonged P-R Interval With Postural Change.*—Of the twenty men whose electrocardiograms showed a prolonged P-R interval, four had a record in which this interval could be altered by change in posture. In Case 1, a reduction occurred in the P-R interval from 0.28 second in the record taken in the recumbent position to 0.20 second in the one taken in the sitting position. The change in position was accompanied by only a slight increase in the heart rate.

In Case 2, the P-R interval decreased from 0.24 second in the record taken in the recumbent position to 0.20 second in the sitting position, without significant change in heart rate.

In Case 3 the routine record revealed negative P waves in all three leads, a P-R interval of 0.24 second, a left axis deviation, a splintered S_3 wave, and a negative T_3 wave (Fig. 1, *A*). One week later additional records were taken in the recumbent position, in the sitting position, in the sitting position following deep inspiration, and in the recumbent position following exercise. The record taken in the recumbent position was the same as the routine record described previously, with a heart rate of 79 per minute. In the sitting position the P

waves in all three leads became positive, the P-R interval was reduced to 0.20 second, and the heart rate was unchanged (Fig. 1, *B*). T_3 was still negative, but the splintering of S_3 had disappeared. This produced a more marked degree of left axis deviation. Deep inspiration in this position did not change the P wave or P-R interval, but reduced the degree of left axis deviation. After one minute of strenuous exercise a record taken in the recumbent position showed negative P waves in all three leads again. The heart rate was increased to 100 per minute and the P-R interval was 0.20 second. Left axis deviation and splintered S_3 were still present, but T_3 was now positive. It appears from the alteration in direction of the P waves that there may have been a shift in the location of the origin of the impulse within the auricle when the airman moved from the horizontal to the vertical position. On physical examination no cardiac abnormality could be detected.



A. *B.*

Fig. 2.—*A*, Case 4, 1940. Recumbent; prolonged P-R interval. *B*, Case 4, 1940. Sitting; normal P-R interval.

Case 4 was a healthy athletic airman, aged 25 years, whose clinical examination revealed no abnormality. Blood pressure was 130/88. Heart size and sounds were normal. The original electrocardiogram, taken in the recumbent position in July, 1940, showed a P-R interval of 0.40 second (Fig. 2, *A*). In the sitting position the P-R interval became 0.20 second (Fig. 2, *B*) with little or no change in the heart rate from that shown in the preceding record.

Additional records were taken in the sitting and recumbent positions, following exercise, and following the subcutaneous administration of $\frac{1}{100}$ grain of atropine sulfate. In the recumbent position the P-R interval was again 0.40 second, and deep inspiration only reduced it to 0.36 second. Thirty minutes after the subcutaneous injection of $\frac{1}{100}$ grain of atropine sulfate the interval in the recumbent position was still 0.36 second.

Nine days later another series of electrocardiographic records was obtained. The man was placed in the recumbent position, and records were taken at various angles by elevating the head of the bed. In the recumbent position the P-R duration was again 0.40 second. At 40 degrees from the horizontal it was still 0.40 second, but at 50 degrees it had changed to 0.20 second. The elevation of the bed was not continuous. There was a pause for several minutes while each

TABLE I. CHANGES IN P-R INTERVAL
(Case 4, 1940)

POSITION	INTERVAL	HEART RATE
Recumbent	0.40	84
25 degrees from horizontal	0.40	82
40 degrees from horizontal	0.40	84
50 degrees from horizontal	0.20	84
60 degrees from horizontal	0.18	84
70 degrees from horizontal	0.20	86
80 degrees from horizontal	0.20	84
Standing	0.20	88
Recumbent	0.40	78
On right side	0.42	66
On left side	0.42	66
Prone	0.44	70
Carotid sinus pressure	0.42	70
Immediately after exercise	0.24	110
Two minutes after exercise	0.36	94
Three minutes after exercise	0.36	96

record was made. Table I shows the P-R interval and cardiac rate in the various positions.

In the right or left lateral or prone positions there was a slight increase in the P-R interval beyond 0.40 second accompanied by a slight decrease in the heart rate. The last three records in Table I were taken immediately after the man had exercised until he was almost exhausted. The heart rate was 110, and the P-R duration was reduced to 0.24 second. A few minutes later the heart rate had decreased to 94, and the P-R interval had increased to approximately 0.34 or 0.36 second. It could not be measured accurately since the P wave was partially superimposed on the T wave.

The remarkable alteration in the P-R interval with change from the recumbent to the upright position was observed over a period of one month. Since there was no evidence of cardiac abnormality other than that found in the electrocardiogram he was permitted to continue his flying training.

An additional electrocardiogram obtained in January, 1942, revealed the same findings with a P-R interval of 0.36 to 0.38 second in the recumbent position. He had been on operational flying overseas as a fighter pilot for several months and showed no clinical evidence of cardiac abnormality. Further examinations were made in April, July, and August, 1943, when the officer was hospitalized for duodenal ulcer. Clinical cardiac examinations at this time were negative, but no electrocardiogram was taken.

On March 3, 1944, after the officer's return to Canada, an electrocardiographic record showed a P-R of 0.34 second, and on March 9, 0.32 second. The latter record was said to have been taken in the sitting position.

On March 28, 1944, he was referred to a consultant cardiologist who reported that in the recumbent position the P-R interval was 0.34 second, and in the sitting position it was 0.32 second. Eyeball pressure did not affect the P-R interval significantly, but after exercise a record in the recumbent position showed it to be 0.19 second with a rate of 108.

On April 17, electrocardiograms were taken by the same cardiologist with the subject in the sitting and recumbent positions before and after the subcutaneous injection of $\frac{1}{50}$ grain of atropine sulfate. In these records the P-R interval was reported to be normal, 0.16 second, in the sitting position and 0.32 in the recumbent. Atropine did not change the P-R interval in either position.

The medical documents therefore report two electrocardiograms with prolonged P-R interval which were said to have been taken in the sitting position,

TABLE II. CHANGES IN P-R INTERVAL—CASE 4—1944

POSITION	P-R INTERVAL (SEC.)	HEART RATE (PER MIN.)	FIGURE
1. Recumbent, normal respiration	0.38	62	Fig. 3, *A*
2. Recumbent, deep inspiration	0.36 to 0.40	60	
3. Recumbent, deep expiration	0.38 to 0.40	64	
4. Sitting, normal respiration	0.20	65	Fig. 3, *B*
5. Sitting, deep inspiration	0.22 to 0.38	74	Fig. 4
6. Sitting, deep expiration	0.24 to 0.38	72	
7. Standing, normal respiration	0.20	82	
8. Lying, right side	0.36	60	
9. Lying, left side	0.36	60	
10. Recumbent, immediately after lying down	0.22	66	Fig. 5
11. Recumbent, 1 minute after lying down	0.38	62	
12. Standing, immediately after exercise (T and P partly superimposed)	0.20 to 0.24	146	
13. Standing, 4 minutes after exercise (T and P partly superimposed)	0.20 to 0.24	130	
14. Eight minutes after exercise, immediately after lying down	0.22 to 0.24	90	
15. Recumbent, immediately after exercise	0.18	90	Fig. 6
16. Recumbent, 3 minutes after exercise	0.20	84	
17. *Tilt Record 1*			
1. From horizontal to 80° in 20 seconds	0.36 to 0.24	70 to 80	
2. At 80° for 10 seconds	0.24 to 0.20	86	
3. From 80° to horizontal in 20 seconds	0.20 to 0.24	76	
4. Horizontal	0.36 immediately	66	
18. *Tilt Record 2*			
1. From horizontal to 80° in 11 seconds	0.36 to 0.34	70	
2. At 80° for 8 seconds	0.30 to 0.20 in 4 seconds		
19. *Tilt Record 3*			
1. From horizontal to 80° in 10 seconds	0.36 to 0.22	66 to 80	
2. At 80° for 10 seconds	0.22	82	
3. From 80° to horizontal in 16 seconds	0.22	80	
4. At horizontal 7 seconds	Still 0.22	70	
20. *Tilt Record 4*			
1. From horizontal to 80° in 18 seconds	0.36 to 0.24 (at 70°)	70 to 80	Fig. 7, *A*
2. At 80° for 10 seconds	0.20	84	
3. From 80° to horizontal in 20 seconds	0.24 to 0.36 (at 10°)	80	Fig. 7, *B*
4. Horizontal for 10 seconds	0.36	72	

but other records taken a few weeks later did not confirm this. A possible explanation for this apparent contradiction was shown in the following series of records obtained in August, 1944. These were taken on a Cambridge electrocardiograph-stethograph (research model). Table II shows the P-R interval as measured in Lead II and the cardiac rate of the records obtained at this time in various postures and phases of respiration.

In electrocardiograms taken after the subject has been in the recumbent position for a few minutes the P-R interval was 0.36 to 0.40 second (Fig. 3, *A*). Records taken in the sitting or standing position had a P-R interval of 0.20 seconds (Fig. 3, *B*). These were similar to records taken four years before (Fig. 2, *A* and *B*). It was noted, however, that when he was tilted from 80 degrees to the horizontal the P-R interval sometimes did not increase for several seconds. For example, in Record 17 the P-R interval increased immediately from 0.24 to 0.36 second as the horizontal level was reached, but in Record 19 the P-R interval was still 0.22 second when the record was stopped seven seconds after reaching the horizontal level. Record 10, taken immediately after the officer lay down, also showed a normal P-R interval (Fig. 5). Apparently the change in P-R interval does not always occur immediately after change in posture. In the same way, on tilting quickly from horizontal to 80 degrees

(Record 18), the P-R remained prolonged for a few seconds before changing to 0.20 second. This may explain the occasional finding of a prolonged P-R interval in records taken in the sitting position, as reported in his medical documents, if these records were taken immediately after sitting up.

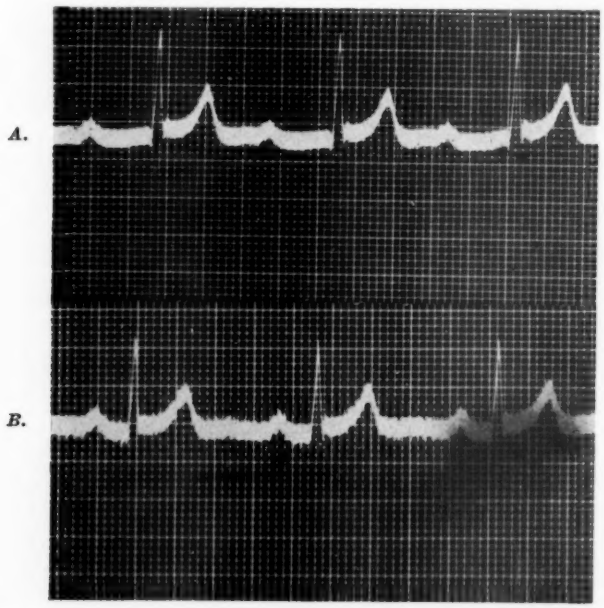


Fig. 3.—*A*, Case 4, 1944, Lead II. Recumbent; P-R, 0.38 second. *B*, Case 4, 1944, Lead II. Sitting; P-R, 0.20 to 0.21 second.

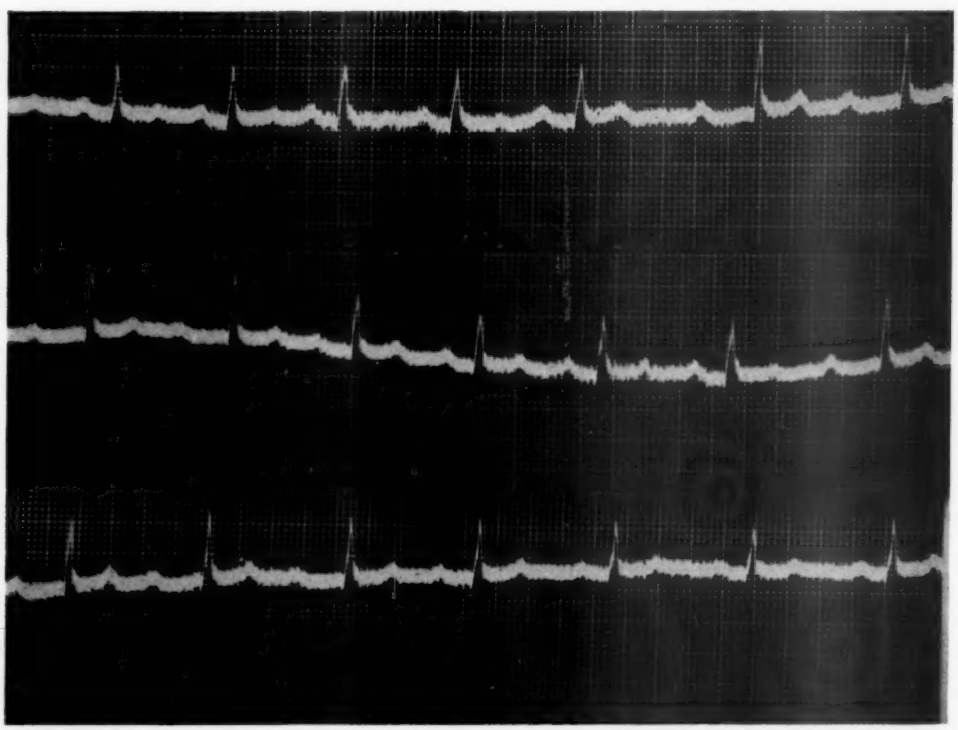


Fig. 4.—Case 4, 1944, Lead II, continuous record. Sitting. Top: P-R increased from 0.22 to 0.38 second with deep inspiration. Middle: P-R decreased to 0.24 second on expiration and increased to 0.38 second on forced expiration. Bottom: P-R returned to 0.22 second with normal respiration.

Deep inspiration and deep expiration both prolonged the P-R interval in records taken in the sitting position (Fig. 4), but no significant change was produced by deep breathing in records taken in the recumbent position where the P-R interval was already 0.36 to 0.38 second.

The exercise carried out before Record 12 consisted of stepping to a chair twenty-five times per minute for three minutes. The electrocardiogram taken while standing showed a P-R interval of 0.20 to 0.24 second immediately after the exercise and four minutes later with the P wave partly superimposed on the preceding T wave. Eight minutes later and immediately after lying down it was still 0.20 second with a rate of 90. It was thought that this short P-R interval in the recumbent position might have been due to the fact that the record was taken soon after the patient assumed the recumbent position and was not due to exercise. However, records were taken on the following day with the subject exercising the legs for two minutes, as in riding a bicycle, while retaining the recumbent position. The pulse rate was increased to 90, and the P-R was reduced to 0.20 second by the exercise alone (Fig. 6). It was apparent,

Fig. 5.

Fig. 6.

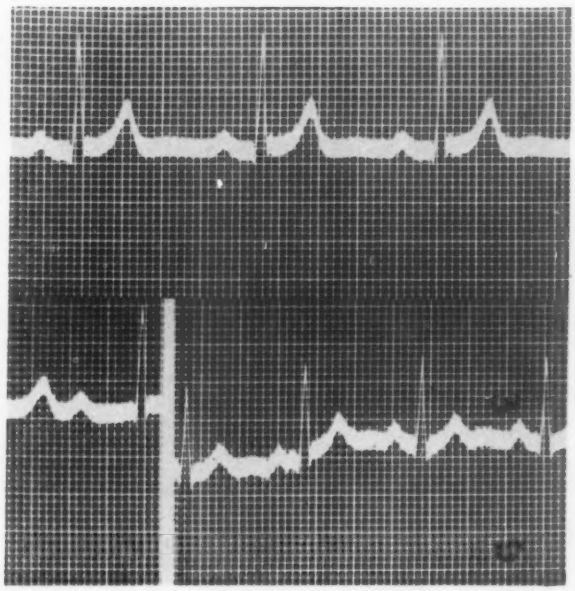


Fig. 5.—Case 4, 1944. Recumbent, immediately after lying down. P-R interval 0.22 second.

Fig. 6.—Case 4, 1944. Recumbent, immediately before and after exercise. P-R interval decreased from 0.36 to 0.18 second.

therefore, that exercise was capable of reducing the P-R to the normal range, even without an excessive increase in rate, while the man remained in the recumbent position. Exercise also resulted in the P-R remaining short if the recumbent position was assumed before the rate had returned to normal. Unfortunately the records were not continued until the change in P-R interval occurred.

During the movement of the tilt table the electrocardiogram was recorded continuously. It was noted that the P-R change usually occurred just as, or shortly after, the body reached the upright or horizontal position, although Record 19 was discontinued before the change occurred. In records taken four years before, the change in P-R interval was noted between 40 and 50 degrees. However, the latter had been taken after a pause at each 10-degree angle, and

TABLE III

POSITION	LEAD I	LEAD II	LEAD III
1. Recumbent, normal respiration	0.13	0.16	0.16
2. Recumbent, deep inspiration	0.14	0.15	0.15
3. Recumbent, deep expiration	0.15	0.16	0.16
4. Sitting, normal respiration	0.14	0.15	0.15
5. Sitting, deep inspiration	0.13	0.15	0.15
6. Sitting, deep expiration	0.14	0.15	0.16

there was a time interval of several seconds sufficient to allow the adaptation of the P-R interval to occur.

B. *Changes in Normal P-R With Postural Change.*—A study was also made of the changes produced by posture and respiration in P-R intervals within the range of 0.12 to 0.18 second. The electrocardiographic records of thirty men were studied, and the results were compared with those of the prolonged P-R group. Electrocardiograms were taken in the recumbent position and the sitting position during normal respiration, following deep inspiration, and following deep expiration. The heart rate and P-R intervals were measured in each record. Table III shows the average duration of the P-R interval with each position.

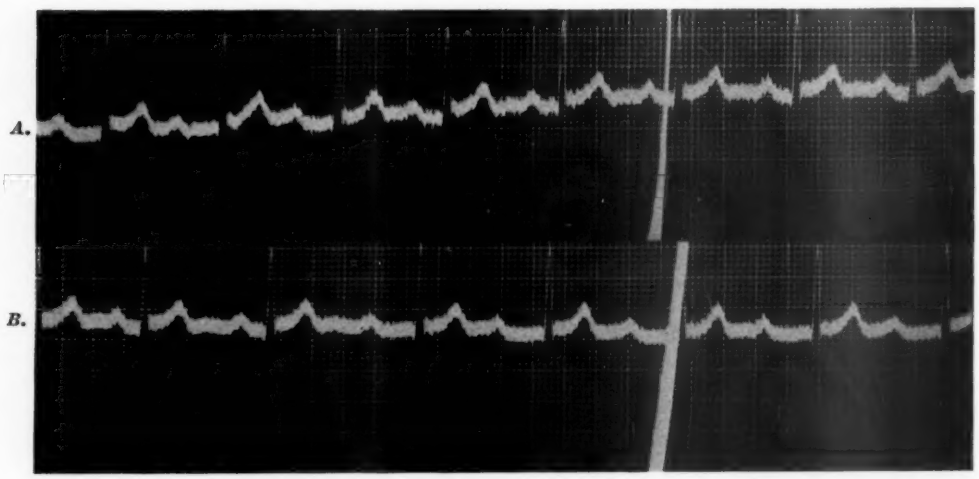


Fig. 7.—*A*, Case 4, 1944. Tilt to 80 degrees (white line). P-R interval decreased from 0.36 to 0.20 second. *B*, Case 4, 1944. Tilt back to horizontal (white line). P-R interval increased from 0.20 to 0.32 second at angle of 10 degrees.

Slight variations in the P-R interval and also the P-wave amplitude occurred in many of the records. This change was usually about 0.01 and 0.02 second. In the records of six men a decrease in P-R interval of 0.02 second accompanied an increase in heart rate produced by a change from the recumbent to the sitting position.

In one other man a P-R interval of 0.18 second and a heart rate of 88 were noted in the record taken in the recumbent position. In the sitting position the rate remained at 88, but the P-R became 0.16 second. On deep inspiration with the man remaining in the sitting position, the interval decreased to 0.12 second. This change is in the reverse direction from that noted in Case 4. The heart rate remained practically the same, 84 per minute, and there was a marked decrease in the amplitude of the P waves with P_3 changing to a negative wave.

DISCUSSION

A number of individuals have shown interesting changes in the P-R interval associated with changes in the posture and respiration and with changes in

heart rate produced by exercise. This study has not produced evidence as to the exact nature of these changes, but it is suggested that two possible explanations might be considered—an aberrant conduction pathway or fluctuation in vagal tone (autonomic imbalance). Lewis[4] and others have shown that increase in the vagal tone in the human being produces many effects on the cardiac mechanism, some of which are seen in the electrocardiogram. These vagal effects are more apparent in convalescent patients, and as a result fainting often occurs.

In this group of four men the first electrocardiograms, taken in the recumbent position, would be considered abnormal insofar as the P-R interval is concerned, while their records taken in the upright position would be considered within the normal limits, or borderline. It is considered possible that the physiologic fluctuations in autonomic balance may be more prominent in these men than in the average individual. The vagal effects might be so marked that the P-R duration would be increased beyond the accepted normal limits. Vagal effects usually produce minor changes such as sinus arrhythmia and brachycardia,[10] but they might be responsible for even greater effects in these individuals. It is not understood why the change in posture should be responsible for the production of such effects.

In electrocardiograms with a P-R interval between 0.12 and 0.18 second, only slight alteration occurred in the P-R duration as a result of change in posture or respiration except in one man whose P-R interval was changed from 0.18 to 0.12 second.

In view of the fact that marked differences can occur in the electrocardiograms of some individuals with change in posture, it is desirable that the position of the patient during the recording of the electrocardiogram should always be noted. It is also suggested that when an electrocardiographic abnormality is found, additional records taken in different positions and phases of respiration may provide further useful information.

SUMMARY

Out of twenty cases with prolonged P-R interval four cases are reported in which definite reduction in the P-R interval occurred on change from the recumbent to the upright position. Similar effects were noted with change in posture and respiration in the electrocardiogram of one man from a group of thirty whose P-R intervals were within the normal limits.

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CONGENITAL HEART DISEASE

Case Reports on Three Members of a Family

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THIS is a report of congenital heart disease in a mother and two of her children. These cases have been considered worth reporting because no similar report has been found in a careful review of the literature.

CASE REPORTS

Case 1.—The mother was 34 years old, white, and somewhat obese; her general health had been good. She had had three full-term pregnancies, each with normal delivery and uncomplicated puerperium. At the time of examination she was able to perform her household duties without difficulty. At the age of 18 she first became aware that she had a "heart condition," and that her blood pressure was elevated.

Family History.—The patient has a sister who has three sons, one of whom died at the age of 8 years of congenital heart disease. Another was rejected by the Air Corps because of a "heart condition," and the third son is on limited service in the Army because of a "heart condition and high blood pressure."

Examination.—Blood pressure, left arm, 210/110; right arm, 190/110. The blood pressure was not obtainable in either leg by the usual methods. The femoral, dorsalis pedis, and posterior tibial pulses were not palpable. There were no dilated vessels on the anterior chest wall, and no unusual pulsations were felt. The heart was not enlarged, and the sounds were of good quality. The pulmonic second sound was louder than the aortic second. The rhythm was normal. There was a short, soft, systolic murmur localized at the base of the heart, and a moderately long, high-pitched systolic murmur was localized to the left of the lower end of the sternum. There were no thrills. There was a moderately palpable suprasternal pulse. There were no signs of decompensation.

Roentgenographic and fluoroscopic examination (Fig. 1) revealed the following: The normal anterior indentation of the esophagus by the aortic knob was not seen after a swallow of barium. This is indicative of hypoplasia of the aorta. The heart size was normal. There was notching of the inferior borders of the ribs posteriorly, between the levels of the fifth through the tenth ribs on the left side, and also a slight degree of notching of the inferior borders of the ribs posteriorly on the right side of the fifth through the ninth ribs.

Laboratory studies, including the electrocardiogram (Fig. 2), were negative.

Case 2.—The daughter, 9 years old, was first known to have had an abnormal heart at the age of 1½ years, after several attacks of tonsillitis. At the time of examination she presented no complaints, and enjoyed all activities without symptoms of diminished cardiac reserve. Two years previously she had an uneventful tonsillectomy.

Examination.—The blood pressure was 80/50. The apex of the heart was in the fifth intercostal space at the anterior axillary line; the pulmonic second sound was louder than the aortic second; and the rhythm was normal. There was a moderately long, harsh murmur occupying all of systole and part of diastole; this was heard over the entire chest, but was loudest at the base and along the left sternal border. There was a marked thrill in the suprasternal notch. The femoral pulsations were normal. There were no signs of decompensation.

Fluoroscopic and roentgenographic studies (Fig. 3) revealed enlargement of the heart involving all of its chambers, especially the left auricle and right ventricle. There was also some enlargement of pulmonary conus; the aortic knob was not visualized.

The electrocardiogram (Fig. 4) revealed right axis deviation, an inverted T wave in Leads II and IV, and moderate elevation of the R-T segment in Lead III. (Inversion of T_1 is considered normal in children.)

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Laboratory investigations, including circulation time (calcium chloride method) and venous pressure, were negative.

CASE 3.—The son, 12 years old, was born a "blue baby," but cyanosis had not been noticed thereafter. At the time of examination he had no complaints; he participated in all activities and showed no evidence of diminished cardiac reserve.

Examination.—Blood pressure, 110/80; the apex beat was felt in the fourth intercostal space, within the midclavicular line; the sounds were of good quality; the pulmonic second was louder than the aortic second; and the rhythm was normal. There was a moderately long, harsh murmur occupying all of systole and part of diastole, heard over the entire chest, but loudest at the base and along the left sternal margin. There was a marked thrill in the suprasternal notch. The femoral pulsations were adequate.

On fluoroscopic and roentgenographic examination of the heart (Fig. 5), slight enlargement of the left auricle and some prominence of the pulmonary conus were noted.*

Laboratory studies, including the electrocardiogram (Fig. 6), circulation time, and venous pressure, were negative.

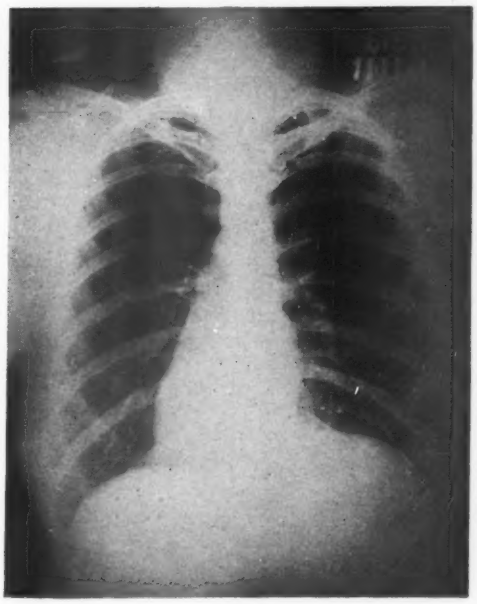

Fig. 1.

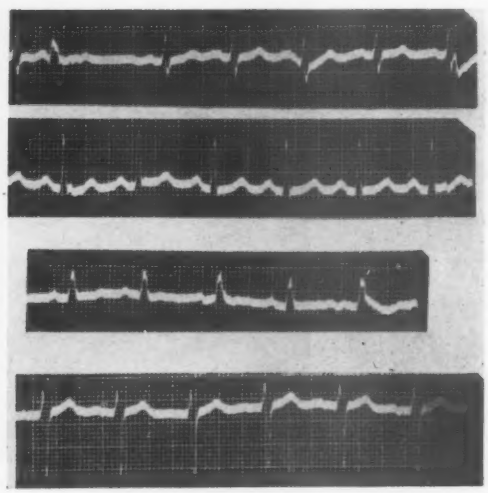

Fig. 2.

Fig. 1.—Mother. (See text for interpretation.)
Fig. 2.—Mother. Normal electrocardiogram; ventricular premature systole in Lead I.

COMMENT

There have been few reports of congenital heart disease in two members of a family.[2-4, 6-8] No reports were found in which three members of a family were afflicted. The family herein discussed presents an unusual number of congenital defects. This becomes even more impressive when the mother's sister's family is included. There is the possibility that between four and seven members of these two families were affected.

The three cases which we have reported include one of coarctation of the aorta in the mother, and patency of the ductus arteriosus in the son and daughter. However, another lesion is most likely present also, for patency of the ductus arteriosus does not explain the enlargement of the left and right auricles. A persistently patent foramen ovale can account for enlargement of

*We are indebted to Major Burt Friedman, M.C., for the interpretations of the roentgenologic studies.

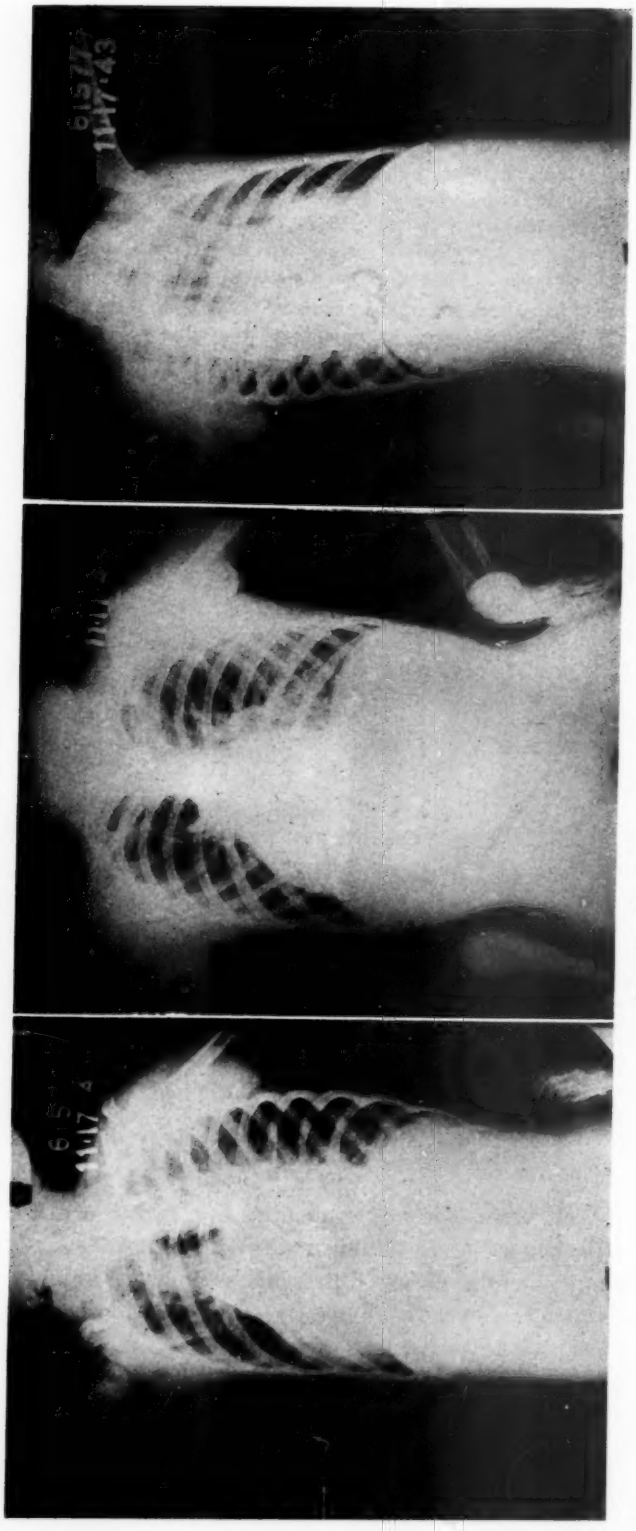

Fig. 3.—Daughter. (See text for description.)

these chambers. In our opinion, the children possess identical lesions, but the daughter has them to a greater degree.

The daughter was the only one to show any degree of cardiac enlargement and an abnormal electrocardiogram (T_2 inverted, indicating myocardial damage). All three, however, were symptom free and apparently were able to carry on their normal daily activities without any difficulty. Although the prognosis must be considered uncertain, it is quite possible that the mother and son may live their full span of years. It is interesting that the mother

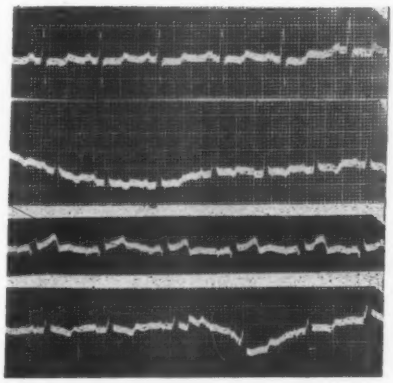

Fig. 4.—Daughter. Note inversion of T wave in Lead II. Right axis deviation.

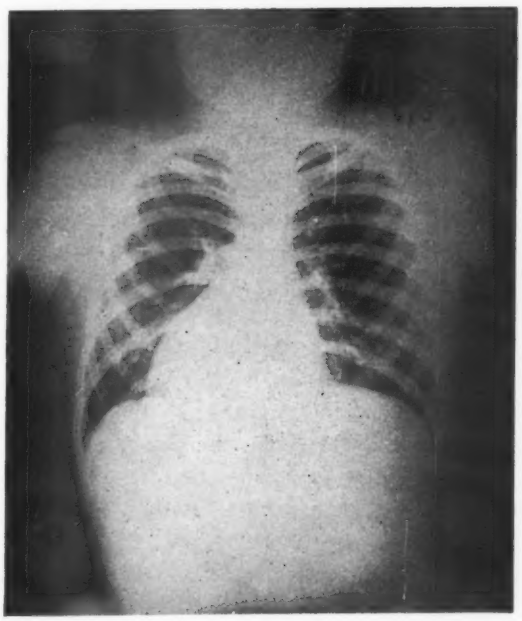

Fig. 5.—Son. (See text for interpretation.)

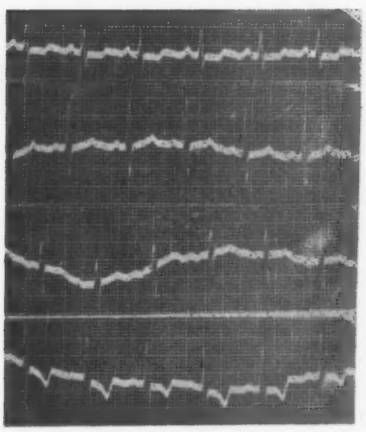

Fig. 6.—Son. Normal electrocardiogram.

went through three pregnancies with normal, spontaneous deliveries. During all of these she never showed any evidence of diminished cardiac reserve. One thus questions the wisdom, at least in this instance, of Walker's recommendation[5] that the method of choice at the onset of labor in women with coarctation of the aorta is cesarean section.

Maude E. Abbott, in her section, "Congenital Cardiac Disease," in McCrae and Osler's *Modern Medicine*,[1] states that, in a series of 850 cases, there was a

history of congenital defect in either a brother or sister of the patient in only eleven cases.

A discussion of the causes of these congenital malformations must of necessity be extremely speculative. Heredity is probably a factor in only a small proportion of cases, for the high mortality rate of congenital cardiac patients would of necessity prevent any direct transmission of these defects in any considerable numbers. However, this possibility must be given due consideration if the history as given by the mother can be considered reliable. And there is no reason to presume otherwise. The factors involved then would probably lie in the presence of genes of a recessive character. According to Abbott,[1] "The predominating cause of the defect is clearly to be sought in the majority of cases in the environment of the developing embryo." She believes that most are due to the arresting of growth at an early stage, before the various portions of the heart have been formed. But some, particularly those in the more fully developed hearts, may be caused by fetal disease.

CONCLUSION

1. The cases of a mother, son, and daughter with congenital heart disease are reported.

2. The infrequency of such a coincidence is pointed out, and a review of the literature is given.

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STRAIN OF THE PECTORALIS MINOR MUSCLE, AN IMPORTANT CAUSE OF PRECORDIAL PAIN IN SOLDIERS

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IN CIVILIANS, coronary arteriosclerosis is so often responsible for precordial pain that the term angina pectoris has come to be applied chiefly to pain of this origin. At this station, on the other hand, if psychoneurosis and anxiety states were excluded, the most common cause of precordial pain was found to be strain of the pectoralis minor muscle. Over a short period of time eight cases of this condition were observed in the hospital and ten cases in the outpatient department. It is therefore the purpose of this communication to describe a hitherto unrecognized clinical entity and differentiate it from both organic and functional disease of the heart and lungs.

Strain of the pectoralis minor muscle may be confused with intrathoracic and cardiac disease more often when the syndrome occurs on the left than on the right side. The initial complaint is pain in the left or right anterior part of the chest. There may be a history of trauma, but frequently the patient is either unaware of any injury or has forgotten it. The pain in the anterior part of the chest is usually in the midclavicular region at the level of the third, fourth, or fifth ribs, and may radiate to the shoulder along the distribution of the muscle, but never radiates down the arm. It may be intermittent and may appear to be brought on by effort. Analysis, however, will always reveal that the effort involves movement of the affected upper extremity. Tenderness is present throughout the distribution of the pectoralis minor muscle, and is maximal in the midclavicular line at the level of the third, fourth, or fifth ribs. It must be remembered, however, that referred tenderness may be present in angina pectoris and in other diseases involving the thoracic cage. An important diagnostic feature is reproduction of the pain in the left anterior part of the chest by having the patient push the upper arm forward against resistance when the elbow is in any position dorsal to the body. The diagnosis can be established beyond doubt if the injection of procaine into the site of maximal tenderness eliminates the pain. Valuable negative evidence is the absence of signs of intrathoracic disease on physical examination and negative electrocardiographic and roentgenologic observations. In addition, heat, massage, and local rest usually cause the pain to subside within several days. In two of the cases observed, the attacks of pain were recurrent and chronic over a period of years. In one of these cases the strain was produced by lifting a dipper full of molten iron, and, in the other, by a fall from a horse.

REPORT OF A TYPICAL CASE

A private, 28 years old, was admitted to the Station Hospital complaining of precordial pain of two days' duration. This pain was in the left anterior part of the chest in the midclavicular region, and radiated to the left shoulder. It was intermittent and apparently brought on by effort. On further questioning, the effort consisted of lifting heavy objects and certain physical exercises in which the left upper extremity was used. In addition, the pain was aggravated by coughing, sneezing, or deep inspiration. There was no

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pain between attacks, although a sense of soreness persisted. No information relevant to the patient's chief complaint was elicited from the past or family history.

On physical examination, tenderness was present in the left anterior part of the chest along the distribution of the left pectoralis minor muscle, and was maximal at the level of the fourth and fifth ribs in the midclavicular line. Bringing the left elbow across the chest toward the right shoulder against resistance did not elicit the pain despite obvious tension produced in the lower portion of the left pectoralis major muscle. When the left elbow was dorsal to the body either above, at a level with, or below the left shoulder, movement of the arm forward against resistance reproduced the left anterior chest pain. Injection of procaine into the site of maximal tenderness in the left anterior part of the chest eliminated the pain completely for several hours and permitted free movement of the left arm without pain in any position. The blood cell count, sedimentation rate, and urine examination, as well as the electrocardiogram and chest roentgenogram, revealed no significant abnormalities.

The patient was kept at rest in bed, and the left pectoral region was subjected to diathermy and gentle massage twice a day. One week after admission he was returned to duty completely free of pain and tenderness.

Since the pectoralis minor muscle has its origin in the midclavicular region of the chest at the level of the third, fourth, and fifth ribs, whereas the pectoralis major originates along the entire parasternal region, this syndrome is probably caused by rupture of a variable number of the fibers of the pectoralis minor from their site of origin on the chest wall, rather than by any injury to the pectoralis major. This is further substantiated by absence of a visible defect or subcutaneous hemorrhage, features usually present in such cases of rupture of the pectoralis major as are described.[1-3] In addition, tension produced in the lower pectoralis major by bringing the arm across the chest fails to reproduce the pain, whereas pushing the arm forward against resistance from a position dorsal to the body, thus bringing the shoulder down and forward, a maneuver effected in part by contraction of the pectoralis minor,[4] does reproduce the pain. Only one case[5] of rupture of the pectoralis minor has been recorded. In this case there was apparently a complete avulsion of the muscle, with the production of a persistent tumor in the pectoral region. In the cases reported in this communication there was a lesser degree of muscle injury more properly called "strain."

Pectoralis minor muscle strain is more common in soldiers than civilians, probably because of the strenuous nature of certain military duties and also because most soldiers are required to participate in calesthenics. This type of strain should therefore be kept in mind, especially in the Armed Forces, whenever a patient complains of left or right anterior chest pain, whether or not it is possible to elicit a history of trauma. It should never be confused with disease of the heart or lungs, or attributed to a psychoneurosis or to "goldbricking." Although several authors have emphasized the importance of distinguishing angina pectoris from muscle strain[6, 7] and from "fibrositis" of the chest wall,[8] none seem to be aware of the specific clinical entity of pectoralis minor muscle strain. This diagnosis may be verified by the simple measures here reported.

SUMMARY

1. Pectoralis minor muscle strain is a common cause of precordial pain in soldiers.

2. Its hitherto undescribed clinical features are discussed and differentiated from organic and functional disease of the heart and lungs.

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ORAL SINGLE-DOSE DIGITALIZATION WITH DIGITALIS LEAF AND DIGITALINE "NATIVELLE"

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WITH THE COLLABORATION OF H. N. GINSBURG, M.D., I. SCHIFF, M.D., AND F. KRAUSE, M.D.

IN A series of reports[1-6] Gold and Cattell and their associates have shown the inadequacy of applying animal assays to man when comparing potency or toxicity of different types of digitalis drugs. A method was developed by them for comparing such drugs in humans by noting the effect upon the S-T-T complex in the electrocardiograms of patients with sinus rhythm, or by determining the degree of slowing of the average resting ventricular rate in patients with persistent auricular fibrillation. They found that an average digitalizing effect was obtained in a few hours when either 15 cat units of U.S.P XI digitalis leaf or 1.2 mg. (3 cat units) of digitaline "Nativelle" were administered as a single dose to patients who had been without any digitalis drug for several weeks; digitalization was obtained with the same dosage of "Nativelle" intravenously as orally. Toxic effects were of the same nature with both drugs; however, with "Nativelle" approximately 2 per cent of the cases showed toxic effects due to local action, and a similar number showed toxic effects due to systemic action when doses of 1.2 mg. were used; while with digitalis about 20 per cent showed toxic effects due to local action, and about 4 per cent showed toxic effects due to systemic action.[4] When 2 mg. of "Nativelle" were used, the incidence of toxicity was much higher than when doses of 1.2 mg. were used.[6]

Digitaline "Nativelle"* is a commercial preparation from *Digitalis purpurea*, considered to contain at least 90 per cent of crystalline digitoxin and to be fairly completely absorbed from the intestine in man.[4, 5]

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*For a discussion of the nomenclature and relation to commercial digitoxin see Gold, Kwit, and Cattell[1] and Gold, Cattell, and associates.[6]

TABLE I

CASE	PATIENT	AGE (YRS.)	SEX	WEIGHT (POUNDS)	DIAGNOSIS	HEART FAILURE	DRUGS GIVEN
1	RS	40	F	100	Rheumatic heart disease, mitral stenosis and insufficiency	Mild	N-D-N
2	JW	44	M	140	Rheumatic heart disease, mitral stenosis and insufficiency	0	N-D-N
3	MH	58	F	130	Rheumatic heart disease, mitral stenosis and insufficiency, aortic insufficiency	Mod. severe	N-D-N
4	ND	68	M	225	Arteriosclerotic heart disease	0	N-D-N
5	MZ	59	F	125	Rheumatic heart disease, mitral stenosis and insufficiency	0	N-D-N
6	SS	29	M	145	Rheumatic heart disease, mitral stenosis and insufficiency	0	N-D-N
7	GL	37	M	180	Rheumatic heart disease, mitral stenosis and insufficiency	0	N-D-N*
8	EF	52	F	110	Rheumatic heart disease, mitral stenosis	0	N-D
9	FD	59	F	125	Arteriosclerotic heart disease	0	N-D-N
10	JO	60	M	155	Arteriosclerotic heart disease	0	N-D-N
11	LS	53	F	100	Rheumatic heart disease, mitral stenosis and insufficiency, aortic insufficiency	Severe	N-D
12	SC	57	F	260	Arteriosclerotic heart disease	0	N-D-N
13	FW	32	M	175	Rheumatic heart disease, mitral stenosis and insufficiency, aortic insufficiency	Severe	N
14	LD	58	F	155	Arteriosclerotic heart disease	Mod. severe	N
15	JF	37	M	148	Rheumatic heart disease, mitral stenosis and insufficiency	0	N-N*

N = Digitaline "Nativelle" orally (1.2 mg.).
D = Digitalis orally (Digitora, ten tablets, each containing 1.28 grains of U.S.P. XII digitalis leaf).
N* = Digitaline "Nativelle" intravenously (1.2 mg.).

The present study was undertaken to confirm for ourselves the safety and comparative efficacy of administering digitalis leaf* and "Nativelle" in single digitalizing doses. Fifteen patients with chronic auricular fibrillation were used in the study (Table I). Of these, all but Patients 8, 11, 13, 14, and 15 received "Nativelle" twice and digitalis once (1.2 mg. of the former and 12.8 grains of the latter). Patients 8 and 11 received "Nativelle" once and digitalis once. Patients 13, 14, and 15 received "Nativelle" only; the last received it once orally and once intravenously; the other two received it only once orally. One of the two "Nativelle" administrations of Patient 7 was made intravenously.

All the patients were kept on a salt-poor diet in the hospital and were ambulatory except for those in severe heart failure. The heart rate was measured daily, for at least a full minute, after twenty minutes or longer of complete rest in bed. When maintenance of an elevated heart rate level indicated fairly complete elimination of previous digitalis drug and acclimatization to the hospital environment, each patient was given the "Nativelle" and kept in bed that day; the heart rate was measured hourly for twelve hours, after which the patient was permitted up and about and daily heart rates were then taken until (in thirteen cases) a new level was reached and maintained before starting upon further therapy.

RESULTS

Oral Administration.—The initial control levels of heart rate prior to the administration of drug ranged from 82 to 159 beats per minute, in most in-

*The preparation of digitalis used was Upjohn "Digitora," of which the "1½ Digitalis Strength" tablet contains 1.28 grains of U.S.P. XII digitalis leaf, equal to 1 cat unit or 0.83 U.S.P. XII Digitalis Units. Ten such tablets comprised the single dose used in all cases.

stances falling below 110. The heart rate levels just prior to administration of the digitalis drugs in those cases receiving two or three courses were for the most part of the same order, so that it was possible to compare the effects of the several courses. The heart rate curves obtained following medication were essentially similar to those obtained under like circumstances by Gold and Cattell and their co-workers both as to amount and time of change. In the patients who had "Nativelle" twice, the two curves were nearly identical, and the whole-leaf digitalis effect was also very much the same (Figs. 1 and 2). The main difference observed was that digitalis leaf tended to depress the rate somewhat more than "Nativelle," and the rate tended to remain low longer and be more delayed in returning to its control level (Fig. 2).

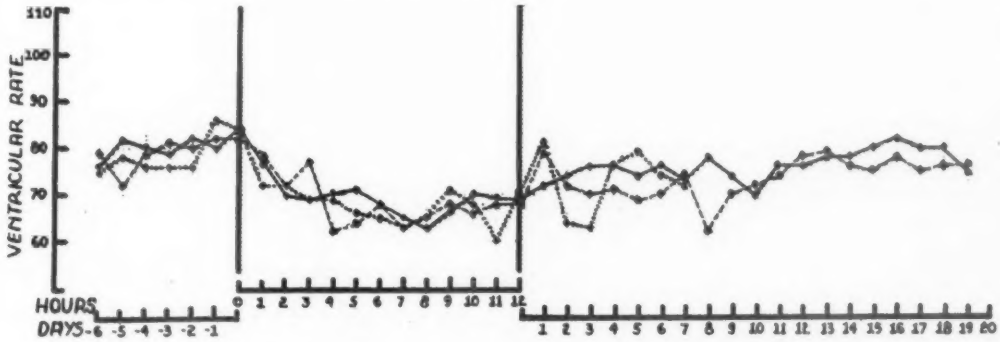

Fig. 1.—Chart listing pertinent data on Patient 4, with arteriosclerotic heart disease, persistent auricular fibrillation, and no heart failure. This patient received at time 0, on different occasions, first, 1.2 mg. of digitaline "Nativelle" (solid-line curve), then 12.8 grains digitalis (dash curve), and then again 1.2 mg. "Nativelle" (dot curve), each in a single oral dose. No difference is seen between the effect of "Nativelle" and digitalis administrations. The heart rate fell from a range of about 83 in about seven hours to a level of about 65, and returned to the control range in about twelve days. Ventricular rate is in beats per minute. Discussed in text.

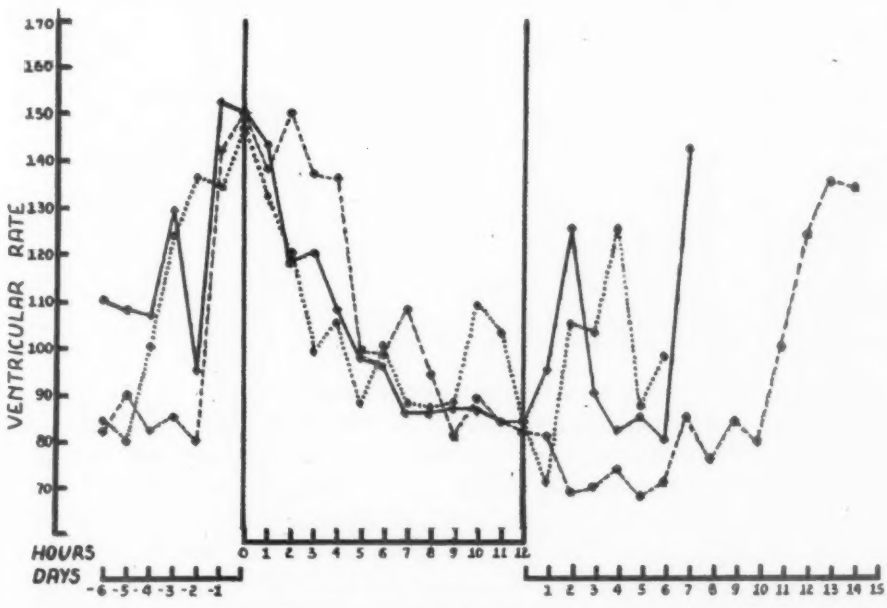

Fig. 2.—Chart listing pertinent data on Patient 6, with rheumatic heart disease, mitral stenosis and insufficiency, persistent auricular fibrillation, and no heart failure. This patient received the same three courses as Patient 4 (Fig. 1) and in the same sequence (conventions as in Fig. 1). Both "Nativelle" and digitalis depressed the rate in five to eight hours from a range of about 150 to one of about 85. With "Nativelle" the heart rate tended to return towards the control level in a few days; with digitalis it remained depressed (even reaching a range of 70 for a few days) for ten days and returned to the control range in twelve days. Discussed in text.

TABLE II

(1) EXPERIMENT	(2) CONTROL LEVEL (BEATS/MIN.)	(3) LOW LEVEL (BEATS/MIN.)	(4) DECLINE (BEATS/MIN.)	(5) PER CENT DECLINE (%)	(6) TIME TO REACH LOW LEVEL (HRS.)	(7) LEVEL OF ½ DECLINE (BEATS/MIN.)	(8) TIME TO REACH ½ DECLINE (HRS.)	(9) TIME TO RETURN TO CONTROL LEVEL (DAYS)
Essential Data on Heart Rate of Twenty-Four Cases of Oral "Nativelle"								
1	124	80	44	35	7	102	3	10
1	122	67	55	45	7	95	2	–
2	99	73	26	26	5	86	2	11
2	97	70	27	28	5	83	2	–
3	108	72	36	33	9½	90	2½	19
3	88	66	22	25	8	77	2½	9
4	84	63	21	25	7	74	1½	16
4	84	63	26	23	7	101	1	–
5	114	88	26	23	7	101	2	11
5	118	90	28	24	8	104	4	–
6	150	86	64	43	7	118	2	8
6	147	87	60	41	7	117	2½	–
7	89	55	34	38	5	72	2	7
8	94	90	4	4	6	92	2	–
9	100	70	30	30	7	85	3	13
9	92	70	22	35	8	86	3	–
10	102	74	28	27	7	88	4	10
10	97	75	22	23	8	86	3	–
11	91	73	18	20	7	82	3½	–
12	96	80	16	17	7	88	2	16
12	91	75	16	18	6	83	3	7
13	105	66	39	37	10	86	4½	–
14	130	73	57	44	10	101	3	–
15	114	71	43	38	4	92	3	10
Average	106	74	32	29	7	90	2½	11
Essential Data on Heart Rate of Two Cases of Intravenous "Nativelle"								
7	89	52	34	38	4	68	1	–
15	96	56	40	42	10	76	1½	–
Essential Data on Heart Rate of Twelve Cases of Oral Digitalis								
1	159	78	81	51	7	118	2½	14
2	90	63	33	37	7	76	1½	15
3	98	60	38	39	6	79	2	20
4	82	64	18	22	4	73	2	21
5	95	55	40	42	10	75	1	31
6	150	85	65	43	9	117	4½	12
7	87	44	43	50	6	66	1½	–
8	101	94	7	7	5	97	3	–
9	94	66	28	33	8	80	2	13
10	93	64	29	31	8	79	2½	13
11	120	90	30	25	6	105	4½	–
12	85	68	17	20	5	76	3	20
Average	104	69	36	33	7	87	2½	18

The figures in this table are obtained by inspection of the curves and are rough approximations based upon the trends of these curves.

In twenty-four trials with "Nativelle" orally (Table II), the rate fell from a level of 84 to 150 (average, 106) in four to ten hours (average, 7) to a level of 55 to 90 (mostly 60 to 80; average, 74), representing a fall in most cases of 15 to 45 per cent (average, 29 per cent). Half the fall occurred in one to four and one-half hours (average, two and one-half hours). The control level was reached again in seven to nineteen (average, eleven) days.

The effects with digitalis leaf were of the same order. In twelve trials with digitalis (Table II) the rate fell from a level of 85 to 159 (average, 104) in four to ten hours (average, seven) to a level of 44 to 94 (average, 69), a fall in most cases of 20 to 40 per cent (average, 33 per cent). Half the fall occurred in one to four and one-half hours (average, two and one-half hours). The control level was reached again in twelve to twenty-one (average, eighteen) days.

While it is important to appreciate the existence of individual variations in response, a composite curve better illustrates the average effect. To accomplish this, the twelve cases which received both drugs were used. The "Nativelle" rates at each time period were first averaged in those cases receiving "Nativelle" twice, then averages of the twelve cases were obtained and plotted as a single curve; the digitalis points were similarly averaged and plotted (Fig. 3). Examination of the curves of averages in this figure shows no essential difference for the first four hours; thereafter, the average rate was somewhat lower with digitalis. The rate remained low for about a week with digitalis, while with "Nativelle" the rate began slowly to rise again after the first day.

Fig. 4 compares the percentage decline in the individual cases. It shows that the decline was greater with digitalis than with "Nativelle" in eleven of the twelve cases.

With both drugs, scatter graphs from data in Table I showed a rough linear trend when the initial level of heart rate (column 2) was plotted against

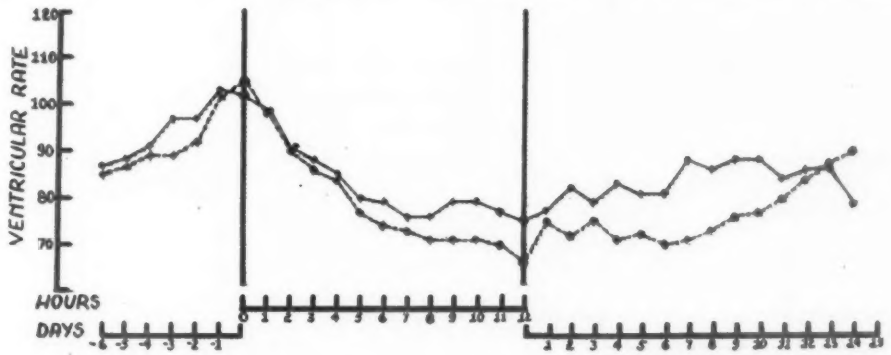

Fig. 3.—Chart showing average heart rates for "Nativelle" (solid-line curve) and for digitalis (dash curve) in the twelve patients receiving both drugs. Discussed in text.

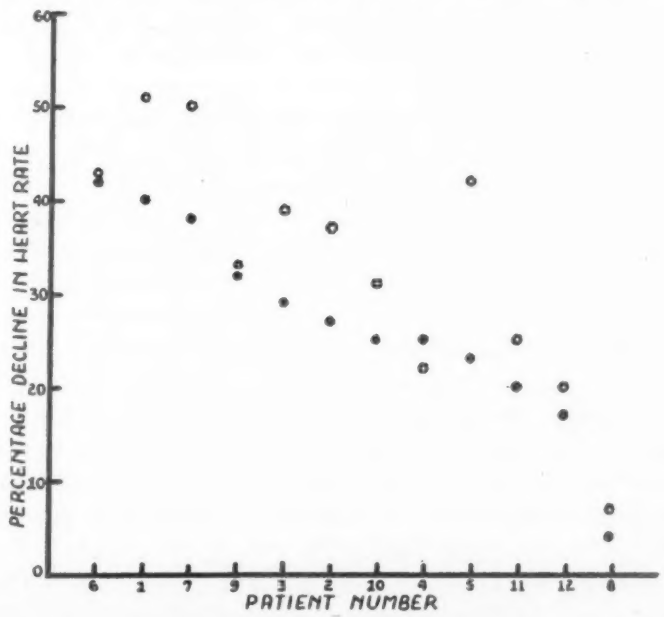

Fig. 4.—Chart showing the percentage decline in heart rate with "Nativelle" (solid circles) and digitalis (open circles) in each of the twelve cases receiving both drugs. The "Nativelle" points in those cases receiving that drug twice are an average of the two courses. Discussed in text.

its low level (column 3), the degree of decline (column 4) and the percentage decline (column 5), respectively. The best trend was obtained in the graph of initial heart rate level plotted against the degree of decline in heart rate. The low level reached tended to be at a faster rate and the actual and percentage decline in heart rate tended to be greater, the greater the initial heart rate. This effect was valuable in that, when initially high, the heart rate tended to reach normal; when low, there was less tendency to decline and go below normal.

Examination of columns 2, 4, 5, 8, and 9 of Table I shows that there is no apparent relationship between the initial level or degree of decline in heart rate, and the time necessary to reach the low level or to return to the control level.

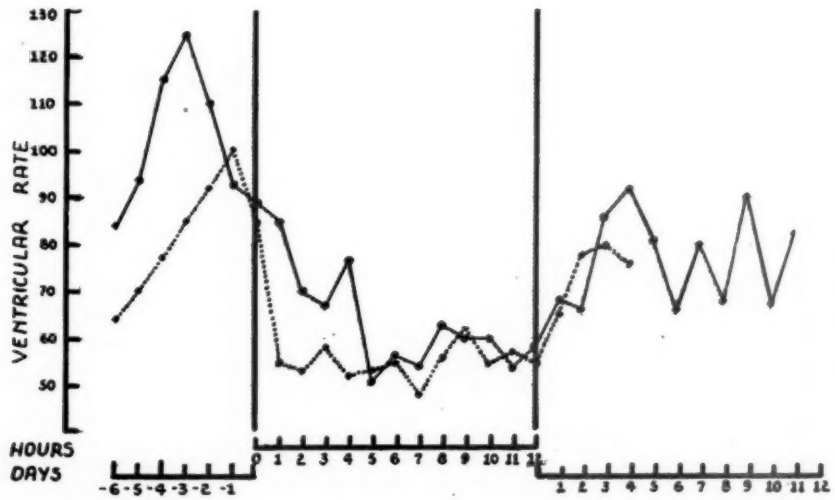

Fig. 5.—Chart listing pertinent data on Patient 7, with rheumatic heart disease, mitral stenosis and insufficiency, persistent auricular fibrillation, and no heart failure. This patient received 1.2 mg. "Nativelle" orally (solid-line curve), then digitalis (not shown), and later 1.2 mg. "Nativelle" intravenously (dot curve). Oral "Nativelle" reduced the heart rate from 89 to a range of 55 in five hours, intravenous "Nativelle" reduced the rate from 84 to the same range in one hour; after five hours the curves were essentially the same. Discussed in text.

Intravenous "Nativelle."—In two cases, the effects of oral and intravenous administration of the same 1.2 mg. dose of "Nativelle" were compared in the same patient. One such experiment is illustrated in Fig. 5. In both cases the initial decline was more rapid than usually occurred with oral "Nativelle." However, after the first three or four hours, the curves were much the same for both intravenous and oral "Nativelle." This is in accord with the observations of Gold and Cattell and their associates.

Toxicity.—In only one of the twenty-six instances was "Nativelle" administration associated with a definite toxic effect; in this instance spotty amblyopia occurred at the second hour. There was also one instance of transitory aching left chest pain at the third hour and one of slight upper abdominal heaviness with belching at the fourth hour. The patient with amblyopia also had a constricting feeling about the chest and a sensation of vigorous heart action during the fifth and sixth hours.

In two of twelve instances (Patients 1 and 11), digitalis leaf administration was associated with vomiting, occurring at the twentieth and twenty-fifth minutes, respectively, and in one of these it occurred again at the second and third hours; however, both patients had nausea and vomiting prior to the admin-

istration of the drug. Both, in spite of the early vomiting, showed a satisfactory reduction in heart rate. One patient had dizziness at the first hour and nausea at the eighth hour, while another had abdominal cramps at the ninth hour.

This incidence of toxic manifestations would appear to be of the same order as that observed by Gold and Cattell and their associates, with similar dosages.

DISCUSSION

Our experience, meager when compared to the large experience of Gold and Cattell and their group, has led us to the following conclusions, which are, in most respects, similar to theirs[6]:

1. Both digitaline "Nativelle" in 1.2 mg. dosage and digitalis leaf in 12.8 grain U.S.P. XII dosage would appear to provide safe, effective, single-dose digitalization in *undigitalized* patients.

2. "Nativelle" has a lower incidence of toxic effects.

3. Intravenous administration of "Nativelle" possesses little advantage over the oral route.

In addition to the above series, about fifteen patients in cardiac failure, most of them without auricular fibrillation, were given 1.2 mg. of digitaline "Nativelle" with good clinical results and no toxic effects. It was sometimes necessary to follow up with further smaller doses before an adequate digitalizing effect was obtained.

From our experience it would appear that single massive oral dosage may be safer than generally realized hitherto, provided *always* that the patient has not had digitalis in the past two or three weeks. Intravenous digitaline "Nativelle" is not the method of choice in these cases, since all the benefits of intravenous use of this drug can be obtained orally. Single dose administration is not advocated as a substitute for intravenous digitalization in cardiovascular emergencies; in such cases strophanthin K or ouabain are the drugs of choice since these drugs act more rapidly than digitaline "Nativelle." However, when an effect is desired in a few hours, the effect can more safely be accomplished by large oral doses rather than by intravenous administration of digitalis preparations. This is the place for single large-dose administration of digitalis.

Even when a moderately rapid effect is desired, we do not advocate single large-dose oral administration as a general rule. In most cases it would be preferable to give the drug in divided doses, such as 0.8 mg. of digitaline "Nativelle" followed by 0.4 mg. in six to eight hours and by such subsequent doses as might be necessary to attain the desired effect. When digitalized, the patient may be maintained on digitalis leaf, "Nativelle," or some other preparation. Average maintenance doses of "Nativelle" are 0.1 to 0.2 mg. daily, more usually the latter.[6]

The similarity of intravenous and oral digitalizing dosage of "Nativelle" is not found with any other digitalis type of preparation; Lanatosid C, for example, requires about ten times as much drug orally as intravenously for rapid digitalization.[2] This, plus the fact that a digitalizing effect is obtained about as rapidly in most cases with oral as with intravenous "Nativelle," suggests that the drug, given orally, is fairly rapidly as well as fairly completely absorbed.

The significant difference found in the time necessary for the heart rate to return to a level range, averaging eighteen days with digitalis and eleven with "Nativelle," and the tendency of the heart rate to retain a low level longer with

digitalis than with "Nativelle" indicate a more rapid excretion or destruction of "Nativelle" than of digitalis leaf.

The actually greater degree of the average depression of heart rate with digitalis than with "Nativelle" is apparently due to the dosage. Thus, Gold and Cattell and their co-workers[3] demonstrated in their time graphs that a greater depression of heart rate occurs with the larger dosage of digitalis when two different doses are compared in the same patient. It would, therefore, appear that 1.2 mg. of digitaline "Nativelle" is equal in potency to somewhat less than 12.8 grains of U.S.P. XII digitalis of the preparation used in our study. This does not agree with the experience of Gold and Cattell and their associates[6] who by the same method, found 1.2 mg. of "Nativelle" approximately equal in potency to 18.5 grains of U.S.P. XII digitalis leaf. The difference may be in the digitalis leaf preparation employed in the two studies.

SUMMARY AND CONCLUSIONS

In order to verify the safety and efficacy of single-dose digitalization and to compare digitalis leaf and digitaline "Nativelle" in this respect, the effects upon the resting heart rate of twelve oral administrations of 12.8 grains of U.S.P. XII digitalis leaf and twenty-four oral and two intravenous administrations of 1.2 mg. of digitalis "Nativelle" were studied in fifteen patients with persistent auricular fibrillation after the manner of Gold and Cattell and their associates.

All administrations had essentially similar effects, causing an average fall in heart rate of about 30 per cent in four to ten (average, seven) hours. Digitalis leaf, in the dosage used, tended to depress the rate somewhat more than "Nativelle" did, and the return to control level was more delayed, averaging eighteen days as compared to eleven days with "Nativelle." With both drugs a greater actual and percentage decline in heart rate tended to occur with greater initial heart rate.

Intravenous "Nativelle" in the two cases where it was used, caused a more rapid decline in rate than oral "Nativelle" but after three to four hours its effect was much the same as that of oral "Nativelle" in the same dosage.

The incidence of toxic manifestations appeared, in this small series, to be of the same order as that observed by Gold and Cattell and their co-workers in a larger series and was less with "Nativelle" than with digitalis leaf.

Either drug in the dosage used would appear to provide a safe, oral, single-dose digitalization, and might be useful when an effect is desired in a few hours in undigitalized patients. This is, in general, preferable to intravenous administration, except in cardiovascular emergencies, where a *Strophanthus* derivate, given intravenously, is preferable for its more rapid effect. While single-dose digitalization was used experimentally, and sometimes therapeutically, divided dosage, such as 0.8 mg. of "Nativelle" followed by 0.4 mg. in six to eight hours, would be preferable in most cases.

The similarity of intravenous and oral digitalizing dose of "Nativelle," found with no other digitalis type of preparation, suggests that the drug, given orally, is fairly rapidly as well as fairly completely absorbed. It would also appear that "Nativelle" is probably more rapidly excreted or destroyed than digitalis leaf.

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CARDIAC ANEURYSM WITH RUPTURE

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ALTHOUGH many cases of cardiac aneurysm have been reported, rupture of aneurysm of the heart as a cause of death is exceedingly rare. Death in this condition is usually due to the underlying heart trouble, such as coronary disease or myocarditis. A case of tuberculous myocardiac aneurysm with rupture has been reported by Jones and Tilden,[1] and a mycotic aneurysm of the heart with rupture has been described by Pirani.[2] Gross and Schwedel[3] reported forty-three cases without an instance of rupture, and Hunter and Benson,[4] in forty cases of spontaneous rupture of the heart, found only one instance in which an aneurysm was the cause. Thomas,[5] in 1930, reported a single case of rupture of aneurysm of the heart. Of fifteen cases of cardiac aneurysm reported by Parkinson, Bedford, and Thomson,[6] none of the seven who died experienced rupture of same. In twenty-one cases reported by Brams and Gropper,[7] rupture did not occur. Friedman and White[18] found no instance of ruptured cardiac aneurysm among 165 cases of chronic or healed myocardial infarction.

Aneurysm of the heart is rarely recognized during life. Brams and Gropper[7] made a clinical diagnosis in only four out of twenty-one cases, and in these four cases the evidence was not positive. Only three of the fifteen cases reported by Parkinson, et al.[6] were discovered before autopsy. Dressler and Pfeiffer[8] reported ten cases in which the condition was perceived during life. Up to 1914 only three cases were correctly diagnosed clinically. Sternberg,[9] Lutembacher,[10] and Christian and Frick,[11] as late as 1939, felt it was difficult if not impossible to diagnose cardiac aneurysm during life.

Nearly all cases are preceded by myocardial infarction due to coronary disease. The resulting fibrosis leaves a weak spot in the heart wall which dilates with the increase of intraventricular pressure. Aneurysm may also occur from abscess of the heart wall, trauma, ulcerative lesions of bacterial endocarditis, or congenital defects (Fulton[12]).

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Working with dogs, Sutton and Davis[13] showed that with adequate rest a much firmer scar was formed after experimental infarction, and the tendency to aneurysm was correspondingly much less than in dogs who did not have the proper rest. They, therefore, felt that adequate rest after coronary thrombosis was of value in preventing the formation of an aneurysm of the heart.

The symptoms and signs may be grouped under (1) clinical, (2) electrocardiographic, and (3) roentgenographic; the latter of which is the most important. There is usually a previous history suggesting coronary thrombosis with infarction. Among the presumptive signs that have been described are enlargement of the heart to percussion; a diffuse and increased area of cardiac impulse, often measuring 7 to 9 cm., with the pulsation more marked between the apex and the sternum than at the apex proper; a small pulse with elevation of intercostal spaces; a systolic murmur just inside the apex; a heavy cardiac thrust associated with a feeble pulse; a wavy pulsation along the inside of the left nipple; gallop rhythm; and a continuous rather severe pain limited to a well-defined area, described by Lutembacher.[10]

According to Brams and Gropper,[7] electrocardiographic studies are of no direct diagnostic aid as they show only the antecedent coronary thrombosis. Several electrocardiographic patterns have been described. Eliaser and Konigsberg,[14] in reviewing five of their own cases and previously published cases of aneurysm of the left ventricle following coronary occlusion, with electrocardiographic studies, found in 27.3 per cent a downwardly directed major deflection in Lead I, with inversion of the T wave and upright P wave, and an upright ventricular complex in Lead III. In 36.4 per cent of these cases the ventricular complexes were directly downwardly in Leads II and III with an upright major deflection in Lead I of either normal or low amplitude. In 18.2 per cent of the cases left bundle branch block was present. Nordenfelt[15] reported the following electrocardiographic characteristics in large chronic aneurysms of the anterior wall of the left ventricle: relatively low R_1, deep S_2 and S_3, elevated S-T segments in all leads, negative T_1, and positive T_2 and T_3. In four cases in which Lead IVF was recorded, R was absent, S was deep, and the S-T segment was elevated with a positive T wave. He feels that if these changes persist over a long period of time, aneurysms or extensive fibrosis of the anterior wall of the left ventricle may be suspected in cases where there is a preceding history of anterior infarction. Thirteen out of fifteen cases reported by Parkinson and his associates[6] showed a T_1 type of infarction, and one showed the T_3 type. In the Dressler and Pfeiffer[8] groups, all cases showed electrocardiographic signs of previous infarction, and deep S deflections in Leads II and III were noted in half of them. In a third of his cases Master[17] found a combination of intraventricular block with a deep Q wave and inverted T wave in Lead I, which he felt suggested the diagnosis of cardiac aneurysm.

The following roentgenographic findings have been described: a circumscribed bulging of the left border of the cardiac silhouette with systolic lateral pulsation; discrepancy between an enlarged left ventricle and a small vascular pedicle (Parkinson, et al.[6]); a broadening of the apex of the heart giving it a square or rectangular appearance; an elongation of the heart to the left; calcification of the aneurysmal sac; evidence of adhesion between the heart and chest wall or diaphragm; and abnormal or absent pulsation of the aneurysmal zone. Aneurysms of the posterior wall of the ventricle are best seen in the left oblique position and may cause a visible displacement of the esophagus. Anterior aneurysms are best seen in the right oblique position. Ledging of the

anterior heart border is of great diagnostic value (Parkinson, et al.[6]). Fluoroscopy may reveal a bulge which is not seen in the roentgenogram. A distention of the anterior wall of the left ventricle, chiefly toward the right, will result in a displacement of the anterior longitudinal sulcus and of the right ventricle. Roentgenkymographic studies may show an aortic type of pulsation along the outer border of the left ventricle (Browne and McHardy[16]). It is very difficult to recognize roentgenologically an aneurysm situated in the apex as it may be buried in the left hepatic lobe or obscured by the diaphragm. This is unfortunate since the apex is the most frequent location for cardiac aneurysms.

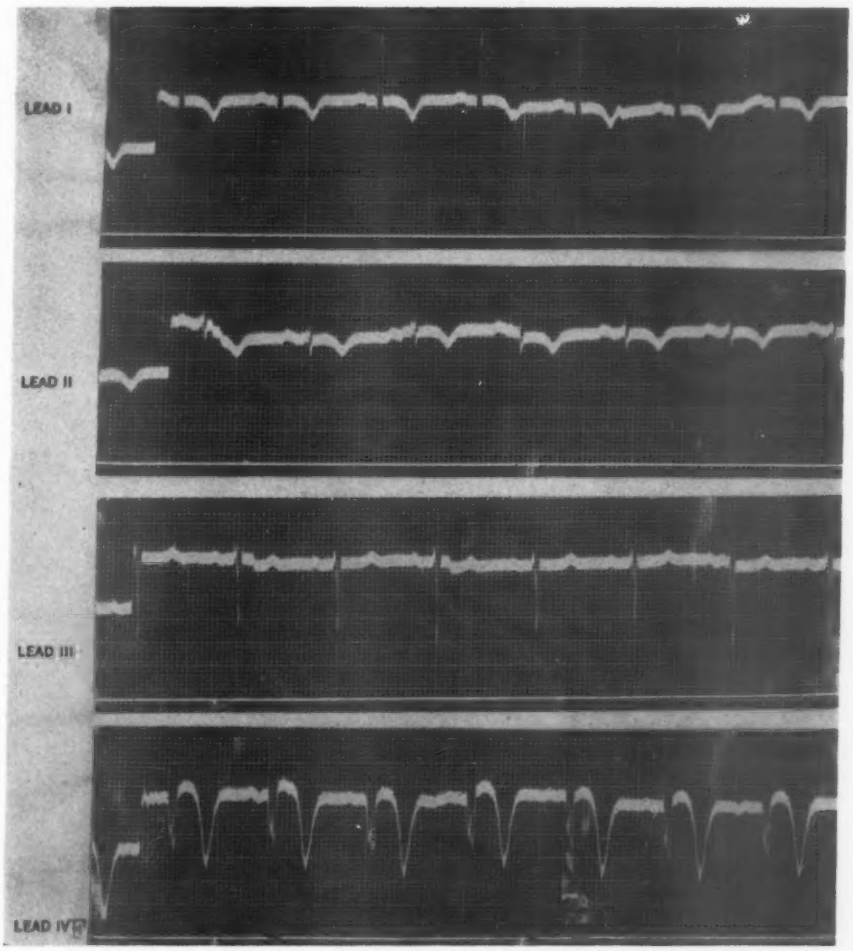

Fig. 1.—Electrocardiogram taken during first admission, showing sharply inverted T waves in Leads I, II, and IV F with major deflections of the QRS complexes directed downwardly in Leads II, III, and IVF; and a marked increase in amplitude of T wave and absent R wave in Lead IVF.

CASE REPORT

A 67-year-old white man stated he was perfectly well until ten days previous to his first admission to the hospital on Feb. 16, 1944. On this day, while shaving, he was suddenly seized with a sharp, severe, precordial pain which forced him to lie down. About one-half hour later he began to vomit and continued to do so intermittently for six hours. There was no previous history of pain in the chest. There was no earlier record of shortness of breath, palpitation, or chronic cough.

Examination revealed an elderly, white man lying quietly in bed. The heart was markedly enlarged both to right and left; the roentgenogram showed its greatest transverse diameter to measure 17 cm. as compared with an internal thoracic diameter of 32 centimeters.

There was a soft systolic murmur at the apex, A_2 was greater than P_2, and the first apical sound was rather distant. The heart rate was 76 per minute, and the rhythm was normal. There was marked dilatation of the aorta. The blood pressure was 134/74. There was sclerosis of the retinal arteries. The prostate gland was slightly enlarged. Otherwise the general physical examination was not remarkable.

At this time the leucocytes numbered 5,200, and the sedimentation rate was 16 mm. in one hour. The Kline test was negative. Electrocardiogram (Fig. 1) was interpreted as evidence of fairly recent previous anterior myocardial infarction with deep S_2 and S_3 waves. The final diagnoses were as follows: generalized arteriosclerotic heart disease with coronary thrombosis and recent anterior infaret; moderate prostatic hypertrophy.

The patient was kept in bed for about four weeks and then gradually was allowed very restricted activity.

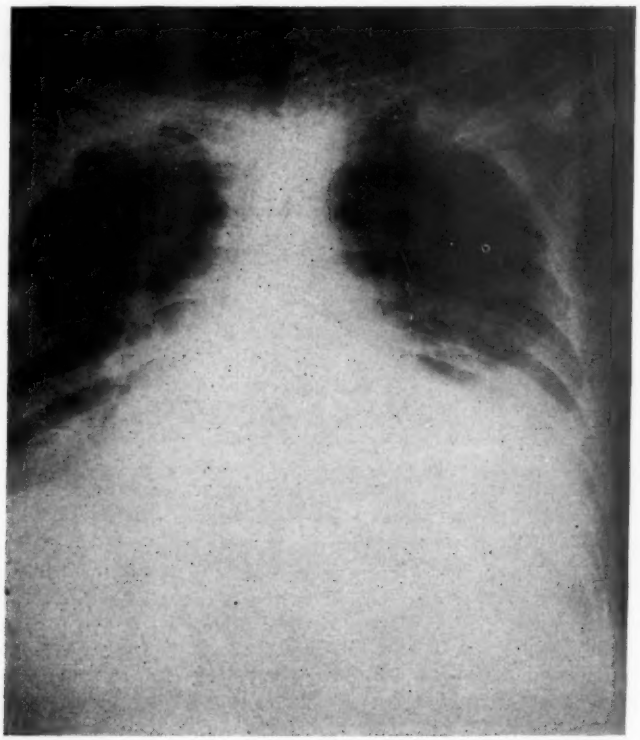

Fig. 2.—Roentgenogram of chest (mobile unit), showing markedly enlarged heart and densities in both lung bases.

He was next seen on April 29, 1944, complaining of a moderate productive cough, spells of pain beginning in the upper abdomen and radiating to the precordial region, accompanied by shortness of breath. At this time the heart was enlarged to the left anterior axillary line. The tones were faint; heart rate was regular, 130 per minute; and the blood pressure was 160/96. There was nothing distinctive about the cardiac pulsations. Moist râles were present at both pulmonary bases with some dullness at the right base. The abdomen was distended, but the liver was not palpable. There was no edema of the extremities.

In the portable x-ray of the chest (Fig. 2) the cardiac borders were difficult to visualize, and the size of the heart was hard to estimate because of the short focal distance. However, there was a bulging of the cardiac apex far to the left. The lung fields had the appearance of extensive pulmonary edema.

Electrocardiogram (Fig. 3) taken on the second day of this admission revealed old anterior myocardial infarction with marked left ventricular preponderance.

Clinical diagnoses were: old arteriosclerotic heart disease with old anterior infarction; generalized arteriosclerosis; benign prostatic hypertrophy; and an added diagnosis of cardiac failure was made.

The patient received 18 grains of digitalis over a period of three days. In the meantime, he developed intermittent pain over the precordial area. A friction rub, which lasted

for one day, was heard in the cardiac apex. The temperature at that time was 100.4° F., the leucocytes numbered 9,450, and the sedimentation rate was 10 mm. in one hour. There was an onset of diarrhea. Suddenly on the sixth day after admission his pulse could not be palpated, he complained of gaseous distention, became comatose, and expired.

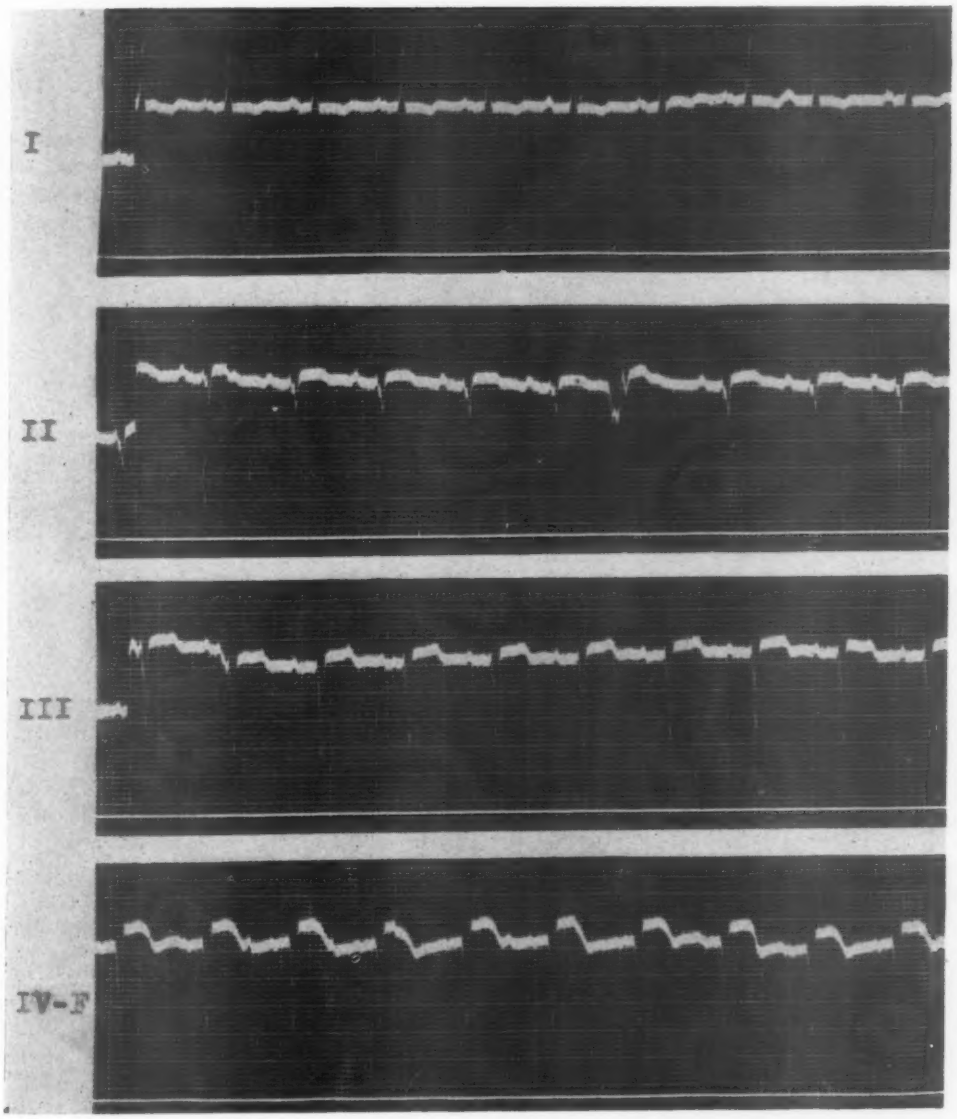

Fig. 3.—Electrocardiogram taken second day of last admission, showing diphasic T waves in Leads I, II, and IVF; slightly elevated S-T segments in Leads II, III, and IVF; and deep S waves in Leads II, III, and IVF, with absence of R wave in Lead IVF.

*Autopsy.**—External appearance: The body was that of a well-developed, well-nourished, white man. There was no rigor mortis, jaundice, or edema. There was cyanosis, Grade 2, of the nails and lips and mild hypostasis. On the anterior chest wall there were several petechiae.

Thoracic cavity: There was no fluid in the thoracic cavity. Adhesions were absent on the left side but present on the right side posteriorly and laterally. The pericardial sac was markedly dilated and filled with blood and blood clots. Crepitus was decreased at both pulmonary bases. The color was a darker red at the bases. Anthracosis, Grade 2, was present.

*Autopsy was performed by Dr. Don Beaver, Director of Pathology, Alexander Blain Hospital, and Woman's Hospital, Detroit, Michigan.

The heart weighed 740 grams. The epicardium was slightly granular and slightly hemorrhagic. At the apex there were dense, fibrous adhesions present which obliterated the pericardial sac. The right auricle was dilated Grade 2. The foramen ovale was closed. The tricuspid valve was normal, the right ventricle was slightly dilated. The muscle was about 1 cm. in greatest thickness. The pulmonary valve was normal. The left auricle was dilated, Grade 2, and the mitral valve was normal. The left ventricle was dilated at the apex into a sac measuring about 8 cm. in diameter. Over the endocardium of the sac there were firm, adherent, blood clots. These were detached with difficulty. The myocardium of the apex, septum, and sac had undergone fibrosis. At one point on the sac the muscle was very thin and soft, and at that point there was a stellate perforation, measuring 1 cm. in length. The right coronary artery was normal at the orifice, but there was considerable calcification of the aorta surrounding the orifice. The vessel itself was large, dilated, and about 3 cm. from its origin there was a patch of arteriosclerosis about 1½ cm. in length;

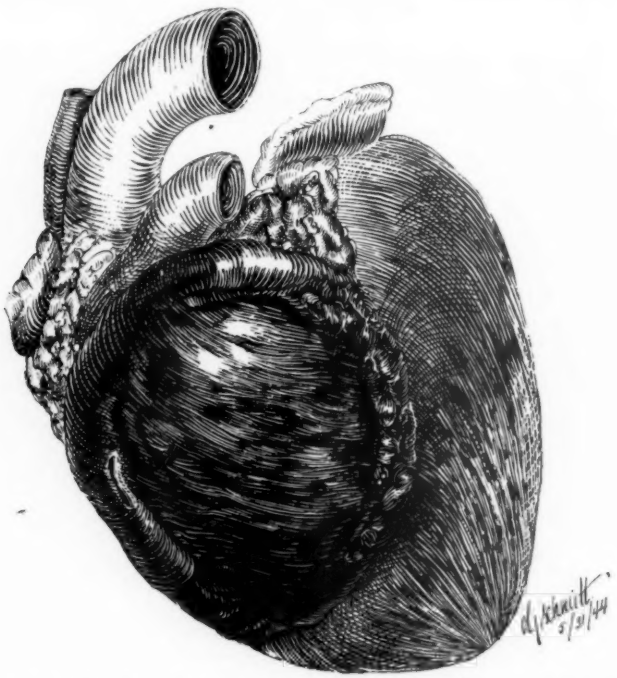

Fig. 4.—Drawing of external surface of heart revealing the saccular aneurysm of the left ventricle, involving the anterior surface. Note the slitlike perforation of the aneurysm at the midportion of the lower margin. The fibrous thickening of the epicardium surrounding the aneurysmal sac is also noteworthy.

however, there was no occlusion at this point. The left coronary artery was normal at the orifice. The circumflex branch was dilated and free from occlusions. The anterior descending branch showed considerable arteriosclerosis and calcification about 1½ cm. from the origin of the vessel. At that point the lumen was occluded by arteriosclerotic changes. No thrombosis was found. The ascending aorta was dilated, Grade 2. The aortic valve cusps were partially calcified, and the valve ring was dilated. The aorta revealed sclerosis, Grade 1, except at the valve ring and around the coronary orifices where it was Grade 2 to 3.

Peritoneal cavity: The spleen weighed 100 grams. There was an old healed infarct about 7 cm. in diameter on the lateral surface. The trabeculae and follicles were distinct. The capsule was smooth.

The left kidney weighed 125 grams. The capsule stripped with ease, revealing a smooth surface which had a small, white area 1 cm. in diameter on the lateral edge. The ureter, pelvis, and medulla were normal. The cortex was normal, except for the white area. The right kidney weighed 125 grams. The capsule stripped with ease, revealing a smooth surface which had a red area 1½ cm. in diameter and a white area 1 cm. in diameter. Except for these two areas, the cortex and medulla were normal. The pelvis and ureter were normal. No further examinating was done.

Microscopic findings: Examination of the heart revealed that the myocardium was atrophic and replaced by scar tissue. At the endocardial margin there was an organizing thrombus. The epicardium was thickened and fibrous.

Anatomic and microscopic diagnoses: (1) Coronary arteriosclerosis with occlusion (anterior descending branch); (2) Healed infarct of apex of left ventricle, with scarring and formation of aneurysm; (3) Recent perforation of the cardiac aneurysm with hemopericardium; (4) Old healed infarct of spleen and kidneys plus recent infarct of right kidney; (5) Old healed pericarditis; and (6) Arteriosclerosis of aorta and aortic valve ring.

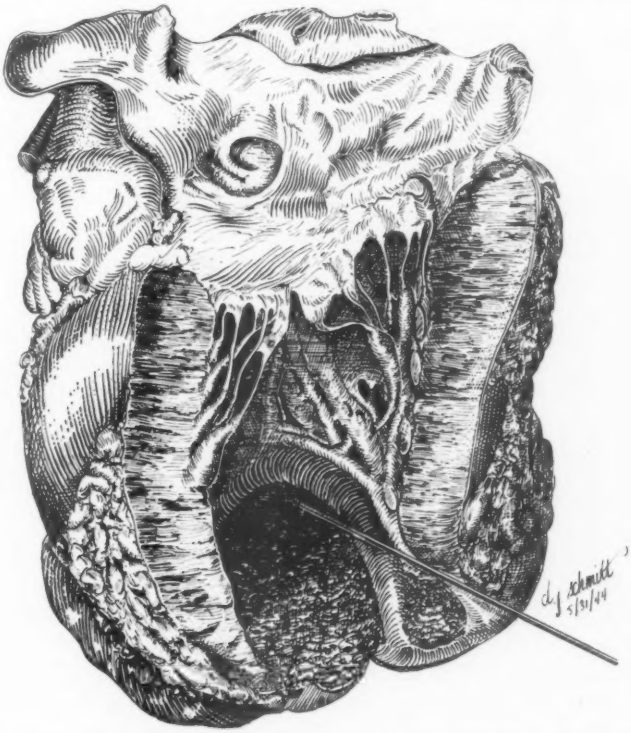

Fig. 5.—Drawing of heart with the left auricle and ventricle opened, disclosing the mitral valve leaflets. The chordae tendineae are attached to anterior and posterior papillary muscles. Aneurysmal dilatation is observed in apical portion of the left ventricle, extending toward the septum and toward the anterior surface below. Note the fibrous thickening of the epicardium over the left ventricle and the aneurysm. Note also the extremely thin muscle which forms the wall of the aneurysmal sac.

DISCUSSION AND SUMMARY

A case of ruptured cardiac aneurysm, verified by autopsy, is reported. The classical signs of aneurysm of the heart are described. However, those which were feasible to look for were not present in this case, making it impossible to diagnose this condition in life. Rupture of cardiac aneurysm is very rare. The electrocardiogram in this case resembled very closely the pattern described by Nordenfelt[15] as diagnostic of cardiac aneurysm of the anterior wall of the left ventricle. When sudden death occurs during the course of coronary heart disease, especially when there has been a history of previous myocardial infarction, rupture of a cardiac aneurysm should be considered. It would seem that adequate rest following myocardial infarction did not prevent the formation of a cardiac aneurysm in this patient.

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THE ELECTROCARDIOGRAM IN HYPERTENSION

I. Its Description

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THE electrocardiogram is of value in the diagnosis and prognosis of hypertension and hypertensive heart disease and may be of value in the determination of suitable cases for surgical treatment of hypertension by splanchnic resection.[1] Changes occurring in the electrocardiogram in hypertension have been described many times;[2-14] however, very few correlations have been made, and changes in the T waves in Leads II and III have rarely been mentioned and have not been stressed. Also there has been but little experience with the multiple precordial leads in hypertension. The surgical treatment of hypertension has afforded us an opportunity to study changes in the electrocardiogram and to make numerous correlations between these and other changes concomitant with hypertension, including pathologic changes in the kidneys.

A. The Limb Leads

Two hundred nine consecutive hypertensive patients, upon whom lumbodorsal sympathectomies were performed by R. H. Smithwick at the Massachusetts General Hospital, were selected for study. One hundred fifty electrocardiograms taken on 132 of the patients were suitable for analysis, that is, each record was taken with the patient in recumbency, and there were no com-

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From the Cardiac Clinic of the Massachusetts General Hospital.

plicating factors such as digitalis effect or congenital or rheumatic heart disease; the additional eighteen records were follow-up electrocardiograms on several of the 132 patients at later dates. The ages of the 132 patients varied from 22 to 58 years with an average age of 40 years. The known duration of hypertension ranged from two months to twenty-four years. Eye grounds and renal biopsies varied from normal to Grade 4. Hearts were normal to large by teleroentgenogram. Electrocardiograms were normal to very abnormal.

One patient was said to have had an acute myocardial infarction about one month before operation, and another patient was said previously to have had a posterior myocardial infarction, but their electrocardiograms showed no evidence of such complications.

We believe that this material represents a good cross section of what one may expect to find in hypertension.

CHANGES IN THE LIMB LEAD ELECTROCARDIOGRAM ASSOCIATED WITH HYPERTENSION

Gross analysis of the 150 electrocardiograms (Table I) revealed that 34.7 per cent were within normal limits, 27.3 per cent had abnormal T waves only, 16 per cent had left axis deviation only, and 22 per cent had left axis deviation and T wave abnormalities. The T wave in Lead I was referred to in this and subsequent tables unless otherwise specified because the most consistent and most marked changes usually occurred in the T wave in that lead. Many times the T waves or axis deviation were within the normal (Fig. 1) but sometimes they were very close to the borderline between normal and abnormal. Occasionally their contours were such that slight adverse alterations in the T wave or electrical axis would have caused them to be abnormal.

Early changes in the electrocardiogram consisted of depression of the RS-T junction, the RS-T segment, and the T wave in Lead I (Fig. 3). In only six of the 150 electrocardiograms did the RS-T junction appear above the isoelectric line. Two of these were not included in Table II because the level of the RS-T junction in Lead III could not be determined accurately in these cases or in the remaining three of the total group of 150. It appeared at the isoelectric line thirty-five times and below that level 106 times. By the time the T wave became zero to 1 mm. in height, the RS-T junction was found above the isoelectric line in only one instance (4 per cent) or below it in nineteen (76 per cent). By the time the T wave became diphasic or inverted, the RS-T junction was found below the isoelectric line in all but one instance when it was at that level (Table III). The most striking changes occurred in the last portion of the RS-T segment and in the first portion of the T wave in Lead I so that the T wave first became diphasic (the minus, plus type) and later inverted. While the T wave was still upright, the RS-T segment was concave upward, but by the time the T wave became completely inverted, the RS-T segment was convex upward; that is, the convexity of the RS-T segment was opposite in direction to that of the T wave.

Concomitant with changes in Lead I were changes in the electrical axis, increase in length of the QT interval, and alterations in the RS-T junctions, the RS-T segments, and the T waves in Leads II and III. When measurable, shifts in the RS-T junctions and segments were found to have occurred in the same direction as those of the T waves. Many times, however, the RS-T junction and segment changes were insignificant and difficult to measure.

TABLE I. GROSS ANALYSIS OF THE LIMB LEADS OF THE ELECTROCARDIOGRAM IN HYPERTENSION

NUMBER OF ECG'S	NORMAL	T CHANGES* ONLY	L. A. D.† ONLY	L. A. D. AND T CHANGES	TOTAL ABNORMAL ECG'S
150	52 (34.7%)	41 (27.3%)	24 (16.0%)	33 (22.0%)	98 (65.3%)
Total number of T changes = 74 (49.3%)					
Total number of L.A.D. = 57 (38.0%)					

*T Changes = T less than 1 mm. in Lead I.
†L.A.D. = left axis deviation of O° or greater (Einthoven's triangle).

Apparently the most common changes in Lead III were elevations of the RS-T junction, the RS-T segment, and the T wave (Figs. 5 and 6). By the time the RS-T junction in Lead I was found below the isoelectric line, the RS-T junction in Lead III was found above the isoelectric line in 41.5 per cent, at that level in 37.7 per cent, and below it in 20.8 per cent (Table II). It was impossible to be certain, however, that the RS-T junction had shifted up or down just because the junction was found to be above or below the isoelectric line. As the last part of the RS-T segment and the first part of the T wave in Lead I became depressed, the last part of the RS-T segment and the first part of the T wave in Lead III frequently became elevated. These alterations often produced "coronary" types of RS-T segments in Lead III (late inversion of the T waves with the RS-T segments at or above the isoelectric line) in electrocardiograms of patients in whom the T waves in Lead III were normally inverted. Not uncommonly, the T wave in Lead III became depressed so that a normally inverted T wave became more inverted. Changes in the T wave in Lead II almost always occurred in the same direction as those in Lead I since changes in Lead I almost always predominated over those in Lead III and Lead II is the algebraic sum of Leads I and III. By the same token, changes in Lead I predominated over those in Lead II in cases in which the T wave was depressed in Lead I and elevated in Lead III. They predominated in Lead II when the T wave was depressed in Lead III, as well as in Lead I.

Concerning inverted T waves per se, the T wave in Lead I was inverted fifty-one times; this abnormality appeared alone twenty-four times, with an inverted T wave in Lead II twenty times, and with inverted T waves in Leads II and III seven times. An inverted T wave in Lead III occurred in fifty-seven cases; alone thirty-six times, with an inverted T wave in Lead II fourteen times, and with inverted T waves in both Leads I and II seven times, as noted previously. *None of the inverted T waves in Lead I alone was associated with abnormal Q waves in Lead I.* Two of the electrocardiograms with inverted T waves in Leads I and II had abnormally large Q waves in Lead III but not in Lead I or Lead II. Neither of these two patients had angina pectoris. Of the seven electrocardiograms with inverted T waves in Leads I, II, and III, none had abnormal Q waves. Four had coronary type T waves in Lead III—late inversion of the T wave with the RS-T junction at or above the isoelectric line. The RS-T junction in Lead I was depressed in each instance. None of these seven patients had angina pectoris. Postoperative follow-up electrocardiograms of five of the seven patients showed improvement in two tracings, no change in two, and adverse change in one. Of the fourteen electrocardiograms with inverted T waves in Leads II and III, only one had possibly abnormal Q waves. The T waves in Lead I were normal in five cases and low (less than 1 mm.) but upright in the other nine. The RS-T junctions in Lead I were depressed in all. Of three patients whose postoperative follow-up electrocardiograms had

returned to normal, all had normally inverted T waves in Lead III. None of these fourteen patients had angina pectoris; however, in two the question of a recent posterior myocardial infarct was raised. The most frequent form of RS-T segment was the one in which the T wave was upright and the RS-T segment was below the isoelectric line and was concave. This form represents 87.3 per cent of the 150 Lead I's, 86.0 per cent of the Lead II's, and 85.3 per cent of the Lead III's. Lead III was the only lead to show a coronary type RS-T segment. Sixteen other forms of the RS-T segment occurred, but their frequency was insufficient to warrant emphasis.

Concerning abnormal Q waves per se, Q waves in Lead I were considered to be abnormally large on two occasions. In one, the Q wave was only 2 mm. in amplitude, but the maximal QRS deflection was only 10 millimeters. In the other, the Q wave was 2½ mm., and the greatest QRS deflection was 13 millimeters. The T waves in Lead I were normal in both. Neither patient had angina pectoris. The Q wave in Lead III was large on fourteen occasions (eleven patients). In three electrocardiograms it was in the form of QS. Small Q waves in Lead II (less than 2 mm.) were present in five of these fourteen cases. The T waves were inverted in Leads II and III in two of the cases. There were no Q waves in Lead II alone.

The QT interval was prolonged above the predicted average normal[15] in almost all of the otherwise abnormal electrocardiograms and in many of the otherwise normal tracings (Table IV).

Changes in the electrical axis occurred simultaneously with those in the T waves in Lead I. Usually the changes were in accord, that is, when the T wave in Lead I became more depressed, the axis shifted more to the left and vice versa. There were many exceptions, however, and the relative change in each varied considerably in different cases.

Changes in the P-R interval or the duration of the QRS complexes may have occurred although these intervals were not prolonged above the range of normal in any record.

CORRELATIONS

In Table II the RS-T junctions in Lead I in 145 of the 150 electrocardiograms were correlated with the RS-T junctions in Lead III. In only four electrocardiograms were the RS-T junctions above the isoelectric line in Lead I. In 106 (73.1 per cent) the junctions were below the isoelectric line, and in 35 (24.1 per cent) they were at that level. From these data it appeared that the depression of the RS-T junction in Lead I was a relatively early and permanent change

TABLE II. CORRELATION OF RS-T JUNCTION IN LEAD I WITH RS-T JUNCTION IN LEAD III

		NUMBER OF ECG'S			NUMBER OF ECG'S
$RS\text{-}T_1$	elevated	4	$RS\text{-}T_3$	elevated	2 (50.0%)
				level	2 (50.0%)
				depressed	0 (0.0%)
$RS\text{-}T_1$	level	35	$RS\text{-}T_3$	elevated	4 (11.4%)
				level	17 (48.6%)
				depressed	14 (40.0%)
$RS\text{-}T_1$	depressed	106	$RS\text{-}T_3$	elevated	44 (41.5%)
				level	40 (37.7%)
				depressed	22 (20.8%)

TABLE III. CORRELATION OF T WAVE IN LEAD I WITH RS-T JUNCTION IN LEAD I

	NUMBER OF ECG'S		
T_1 0 to 1 mm.	25	$RS\text{-}T_1$	+ 1 (4.0%) 0 5 (20.0%) − 19 (76.0%)
T_1 diphasic or inverted	49	$RS\text{-}T_1$	+ 0 (0.0%) 0 1 (2.0%) − 48 (98.0%)

in the electrocardiogram in hypertension. Electrocardiograms with the RS-T junction above the isoelectric line in Lead I were so few that a statistical analysis of the associated levels of the RS-T junction in Lead III was of little value. When the junction was at the isoelectric line in Lead I, it appeared below that level in Lead III four times as frequently as it did above it. By the time the RS-T junction was below the isoelectric line in Lead I, the junction appeared above that level in Lead III twice as often as it did below it. From these data, it appeared that elevation of the RS-T junction was the most common change in Lead III.

In Table III the RS-T junction in Lead I was correlated with the height of the T wave in that lead. When the T wave measured in height from zero to 1 mm., the RS-T junction appeared above the isoelectric line only once (4 per cent). By the time the T waves became diphasic or inverted, all but one (98 per cent) of the RS-T segments appeared below the isoelectric line, and none appeared above it. These data substantiate the permanency of the RS-T junction depression and afford important information for the differential diagnosis between the electrocardiogram in hypertension and that in coronary disease.

The QT interval was correlated with other findings in the electrocardiogram in Table IV. Many times the end point of the QT interval was not clear-cut, but it was possible to obtain reasonably accurate measurements in 138 records. The measured QT interval was compared with the predicted normal interval and the range of normal. When the QT interval was at the predicted normal or below, 81.3 per cent of the electrocardiograms were normal otherwise, and when the QT interval was above the range of normal 72.6 per cent were abnormal otherwise.

Table IV may be broken down another way as follows: of the fifty-two normal electrocardiograms, 25 per cent had QT intervals at or below the predicted normal, 30.8 per cent above the predicted average normal but within the range of normal, and 44.2 per cent definitely above the normal range. Of the eighty-six electrocardiograms which were abnormal otherwise, only 3.5 per cent had QT intervals which were at or below the predicted normal while 25.6 per

TABLE IV. CORRELATION OF THE QT INTERVAL WITH OTHER CHANGES IN THE ELECTROCARDIOGRAM

THE QT INTERVAL	NUMBER OF ECG'S (*138*)	NORMAL (*52*)	T CHANGES ONLY	L.A.D. ONLY	T CHANGES AND L.A.D.	TOTAL OF ABNORMAL ECG'S (*86*)
1. Predicted normal or below*	16	13 (81.3%) (*25.0%*)	0 (0%)	1 (6.2%)	2 (12.5%)	3 (18.7%) (*3.5%*)
2. Above predicted normal but within normal range	38	16 (42.1%) (*30.8%*)	8 (21.0%)	5 (13.2%)	9 (23.7%)	22 (57.9%) (*25.6%*)
3. Above normal range	84	23 (27.4%) (*44.2%*)	25 (29.8%)	18 (21.4%)	18 (21.4%)	61 (72.6%) (*70.9%*)

*As determined by the prediction table of Ashman and Hull.[15]

cent had QT intervals above the predicted normal but below the upper limit of normal, and 70.9 per cent had QT intervals above the range of normal.

Electrocardiographic changes were correlated with eye-ground findings in Table V. Criteria for grading the eye grounds were as follows: normal, no abnormal findings in the retina; Grade 1, minimal caliber changes in the retinal arterioles; Grade 2, caliber changes with arteriovenous nicking; Grade 3, hemorrhages and exudates; Grade 4, changes as in Grade 3 plus papilledema. Eliminating one electrocardiogram in which the eye grounds were normal, there was a tendency for the electrocardiogram to become more abnormal as the eye grounds became worse.

TABLE V. CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH THE EYE-GROUND CLASSIFICATION

EYE GROUNDS	NUMBER OF ECG'S	NORMAL	T CHANGES ONLY	L.A.D. ONLY	T CHANGES AND L.A.D.	TOTAL ABNORMAL ECG'S
Normal	1	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)
Grade 1	44	23 (52.3%)	7 (15.9%)	5 (11.3%)	9 (20.5%)	21 (47.7%)
Grade 2	29	12 (41.4%)	9 (31.0%)	3 (10.4%)	5 (17.2%)	17 (58.6%)
Grade 3	50	12 (24.0%)	15 (30.0%)	9 (18.0%)	14 (28.0%)	38 (76.0%)
Grade 4	26	5 (19.2%)	9 (34.6%)	7 (26.9%)	5 (19.2%)	21 (80.7%)

In Table VI changes in the electrocardiogram were correlated with pathologic findings in the renal biopsies. The biopsies were classified into five groups as follows: Grade 0, no abnormal findings seen; Grade 1, slight amount of vascular change (predominantly arteriolar intimal hyalinization and arterial endothelial hyperplasia); Grade 2, slightly more vascular change than in Grade 1, and an occasional hyalinized glomerulus; Grade 3, severe vascular disease in every vessel with predominant medial arteriolar hypertrophy and many hyalinized glomeruli; Grade 4, involvement of every vessel, scarring of many glomeruli and atrophy of surrounding tubules.[16] There appeared to be no definite positive correlation between alterations in the electrocardiogram and pathologic changes in the kidney except that, in the group with Grade 4 kidneys, the incidence of abnormal tracings was distinctly greater than in the other groups.

Correlations with the heart size were made in Table VII. The heart size in each instance was based on the roentgenologist's opinion with the addition of

TABLE VI. CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH RENAL BIOPSIES

RENAL GRADE	NUMBER OF ECG'S	NORMAL	T CHANGES ONLY	L.A.D. ONLY	T CHANGES AND L.A.D.	TOTAL ABNORMAL ECG'S
0	8	3 (37.5%)	2 (25.0%)	1 (12.5%)	2 (25.0%)	5 (62.5%)
1	20	7 (35.0%)	4 (20.0%)	3 (15.0%)	6 (30.0%)	13 (65.0%)
2	29	9 (31.0%)	9 (31.0%)	5 (17.2%)	6 (20.7%)	20 (68.9%)
3	36	14 (38.9%)	10 (27.8%)	3 (8.3%)	9 (25.0%)	22 (61.1%)
4	20	3 (15.0%)	5 (25.0%)	4 (20.0%)	8 (40.0%)	17 (85.0%)

TABLE VII. CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH HEART SIZE BY TELEROENTGENOGRAM

HEART SIZE	NUMBER OF ECG'S	NORMAL	T CHANGES ONLY	L.A.D. ONLY	T CHANGES AND L.A.D.	TOTAL ABNORMAL ECG'S
Normal	47	18 (38.3%)	14 (29.8%)	7 (14.9%)	8 (17.0%)	29 (61.9%)
Rounded apex (otherwise normal)	32	13 (40.6%)	6 (18.75%)	7 (21.9%)	6 (18.75%)	19 (59.4%)
Definitely enlarged	58	12 (20.7%)	18 (31.0%)	10 (17.3%)	18 (31.0%)	46 (79.3%)

measurements. There were a few more abnormal electrocardiograms in the group with enlarged hearts than in the group with normal hearts but no striking correlation was found. The T changes noted in the table relate to Lead I, as already stated.

Inverted and diphasic T waves in Lead II were also correlated with the heart size, and 39.4 per cent of the patients with abnormal T waves in Lead II were found to have hearts of normal size.

The electrocardiographic changes were correlated with the symptoms of chest pain and dyspnea in Table VIII. In the group in which the patients complained of dyspnea only, the number of abnormal electrocardiograms was not significantly greater than in the group without dyspnea. This was not true of the group with chest pain—by the time patients complained of chest pain, the electrocardiogram was abnormal in each instance. Abnormal T waves appeared in Lead I or II in 91.7 per cent of the cases. It so happened that none of the patients complaining of chest pain had abnormal Q waves or diphasic or inverted T waves in Leads I, II, and III, or in Leads II and III.

TABLE VIII. ELECTROCARDIOGRAPHIC CHANGES CORRELATED WITH CHEST PAIN AND DYSPNEA

SYMPTOMS	NUMBER OF ECG'S	NORMAL	T CHANGES ONLY	L.A.D. ONLY	T CHANGES AND L.A.D.	TOTAL ABNORMAL ECG'S
Dyspnea	50	16 (32.0%)	14 (28.0%)	8 (16.0%)	12 (24.0%)	34 (68.0%)
Pain	11	0 (0%)	6 (54.6%)	1 (9.0%)	4 (36.4%)	11 (100%)
Dyspnea and pain	1	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)
No dyspnea or pain	87	36 (41.4%)	21 (24.1%)	15 (17.3%)	15 (17.3%)	51 (58.6%)

In Table IX, electrocardiographic changes were correlated with the known duration of hypertension, and there appeared to be no definite relationship.

TABLE IX. CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH THE KNOWN DURATION OF HYPERTENSION

YEARS DURATION	NUMBER OF ECG'S	NORMAL	T CHANGES ONLY	L.A.D. ONLY	T CHANGES AND L.A.D.	TOTAL ABNORMAL ECG'S
1	36	10 (27.8%)	12 (33.3%)	4 (11.1%)	10 (27.8%)	26 (72.2%)
2	19	7 (36.8%)	6 (31.6%)	3 (15.8%)	3 (15.8%)	12 (63.2%)
3	14	5 (35.7%)	2 (14.3%)	3 (21.4%)	4 (28.6%)	9 (64.3%)
4	16	7 (43.8%)	2 (12.5%)	5 (31.2%)	2 (12.5%)	9 (56.2%)
5	28	9 (32.1%)	11 (39.3%)	3 (10.7%)	5 (17.9%)	19 (67.9%)
10	23	11 (47.8%)	5 (21.7%)	4 (17.4%)	3 (13.1%)	12 (52.2%)
15	4	3 (75.0%)	0 (0%)	0 (0%)	1 (25.0%)	1 (25.0%)
20	7	0 (0%)	3 (42.8%)	2 (28.6%)	2 (28.6%)	7 (100%)
25	1	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)

In Table X, electrocardiographic changes were correlated with the diastolic blood pressure on admission and no definite positive relationship was observed.

TABLE X. CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH THE DIASTOLIC BLOOD PRESSURE ON ADMISSION

DIASTOLIC PRESSURE	NUMBER OF ECG'S	NORMAL	T CHANGES ONLY	L.A.D. ONLY	T CHANGES AND L.A.D.	TOTAL ABNORMAL ECG'S
90 or below	3	2 (66.7%)	1 (33.3%)	0 (0%)	0 (0%)	1 (33.3%)
91 to 120	53	19 (35.8%)	11 (20.8%)	10 (18.9%)	13 (24.5%)	34 (64.2%)
121 to 140	61	19 (31.1%)	16 (26.2%)	10 (16.4%)	16 (26.2%)	42 (68.8%)
Over 140	31	12 (38.7%)	12 (38.7%)	4 (12.9%)	3 (9.7%)	19 (61.3%)

In Table XI, electrocardiographic changes were correlated with the body build. This table is of interest in that nine (60 per cent) of the fifteen thin patients had T-wave changes without abnormal axis deviation, one (6.7 per cent) had T-wave changes and left axis deviation, five (33.3 per cent) had normal electrocardiograms, and none had left axis deviation without T-wave changes. In the short and fat or stocky groups, only five (19.2 per cent) had T-wave changes alone while nine (34.6 per cent) had axis and T-wave changes and five (19.2 per cent) had left axis deviation alone. Some of the patients who were described as stocky or short and fat were basically of thin build—the midclavicular line of one patient labelled as short and stocky was only 6.5 centimeters from the midsternum. This partially explains why some of these patients had T-wave changes without axis change.

TABLE XI. CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH THE BODY BUILD

BODY BUILD	NUMBER OF ECG'S	NORMAL	T CHANGES ONLY	L.A.D. ONLY	T CHANGES AND L.A.D.	TOTAL ABNORMAL ECG'S
Thin	15	5 (33.3%)	9 (60.0%)	0 (%)	1 (6.7%)	10 (66.7%)
Average	109	40 (36.7%)	27 (24.8%)	19 (17.4%)	23 (21.1%)	69 (63.3%)
Short and fat or stocky	26	7 (26.9%)	5 (19.2%)	5 (19.2%)	9 (34.6%)	19 (73.1%)

DISCUSSION

It is unlikely though remotely possible that the earliest change in the electrocardiogram in hypertension is an elevation of the RS-T segment in Lead I, as described by Robb and Robb.[14] If this occurred in our series it must have been early and transient since in only six of the 150 electrocardiograms were the RS-T junctions found above the isoelectric line. The depression of the RS-T segment in Lead III in certain cases of hypertension could not with certainty be explained by strain on various muscle bundles as described by Robb and Robb; however, some such strain is probably the cause. Those workers found a depression of the RS-T segments in all three leads following a sudden rise in the pressure in the right ventricle in experimental animals, and it is possible that an acute rise in the pressure in the left ventricle may also produce similar changes. All of our patients with depressed RS-T segments in all leads had diastolic blood pressures between 130 and 160 mm. Hg except one, and this patient had a diastolic pressure of 115 mm. of mercury.

Lengthening of the QT interval has been previously described as an early manifestation of hypertension[15]; it may well be associated with enlargement—a stretching and hypertrophy of the muscle fibers.

As stated before, electrocardiographic alterations in hypertension have been mentioned many times.[2-14] Inversion of the T wave in Lead I and axis changes have been usually stressed. Rykert and Hepburn[10] presented an early and important paper calling attention to the fact that inversion of the T wave in Lead I can result from hypertension alone without coronary heart disease per se. Only rarely have changes in the T waves in Leads II and III, or I, II, and III been mentioned, however, and never have they been stressed. Depression of the RS-T segment in Lead III has not been described. Willius reported 130 cases in which there was negativity of the T waves due to any cause and upon which autopsies were performed. Fifty-four of the patients had hypertensive heart disease. Electrocardiograms of thirteen (25 per cent) of these patients showed inverted T waves in Leads I, II, and III, and five (9.6 per cent) showed inverted T waves in Leads II and III. Ninety-two per cent of all patients

with negative T waves in Leads I, II, and III from any cause showed 1 to 4 plus sclerosis of the coronary vessels and 69 per cent of those with inverted T waves in Leads II and III showed coronary sclerosis. Barnes and Whitten,[7] reporting on 117 patients with significant T wave changes, upon whom necropsies were performed, mentioned that 7 per cent showed inversion of the T waves in Leads II and III, and 9.4 per cent showed inversion in Leads I, II, and III. They stated that when inversion of T waves occurred in Leads II and III, one should suspect some condition causing an overload on the right ventricle or a posterior myocardial infarction. Kaplan and Katz[13] stated that ten of fifty-two records with axis deviation and T-wave changes differed from the classical pattern in that the T wave in Lead III was inverted. Some of the books on electrocardiography,[15, 17-19] have stressed the changes in the T wave in Lead I but not those in II and III. Several of the electrocardiograms in hypertension presented by Katz[19] had abnormal T waves in the three standard leads, and one showed striking depression of the RS-T segments and T waves in the three leads.

It is not difficult to visualize why inversion of the T waves occurs in Leads II and III or later in Leads I, II, and III in patients who have normally inverted T waves in Lead III when marked changes occur in Lead I and little or no changes occur in Lead III or when there is depression of the RS-T segments in Lead III, as well as in Leads I and II. The facts that they may occur in the electrocardiograms of young people who are not suspected of having coronary disease and do not have angina pectoris, that they are not associated with abnormal Q waves, and that the electrocardiogram may return to normal with a normally inverted T wave in Lead III following sympathectomy lend support to the theory that changes in the T waves in Leads II and III alone, or in combination with changes in the T wave in Lead I,[20] may be caused by hypertension, per se, without coronary disease or superimposed right ventricular strain; heart position related to body build is undoubtedly an important factor in these cases as it is in the cases to be mentioned.

Superimposed right ventricular strain has held an important place in the explanation of T-wave changes without left axis deviation. A few investigators, especially Wilson et al.,[5, 21] have emphasized the role that position of the heart within the thorax plays in this picture. Special emphasis on alterations of the T wave in Lead II with changes in the position of the body have been reported several times.[22, 23] Knowing that body build greatly influenced the position of the heart within the thorax we correlated electrocardiographic changes with the body build. Since T-wave and axis changes occur in the electrocardiogram in hypertension, it is logical to assume that a vertically placed heart or one so rotated that the electrical potential of the left ventricle is transmitted to the left leg would develop abnormal T waves before it would left axis deviation and that in a transversely placed heart or one so rotated that the potential of the left ventricle is transmitted to the left arm, left axis deviation without abnormal T waves is likely to occur. These assumptions were quite well supported by our data. Of fifteen patients, who were of thin build, nine (60 per cent) showed T changes only, one showed abnormal T waves and left axis deviation, and none showed left axis deviation without abnormal T waves. Of twenty-six patients, who were short and fat, or stocky, five (19.2 per cent) had left axis deviation without abnormal T waves, nine (34.6 per cent) had left axis deviation and abnormal T waves, and five (19.2 per cent) had abnormal T waves without left axis deviation. T-wave abnormalities without left axis deviation may be accounted for in several ways: (1) a tendency for T waves to become markedly altered before significant axis changes appear in certain

individuals when there are sudden rises in intraventricular pressure; (2) rotation of the heart in some stocky persons so that the electrical potential of the left ventricle is transmitted to the left leg; and (3) misinterpretation of body build. Some patients who are short and fat and appear to be stocky are fundamentally of thin build as to thorax. The midclavicular line of one of our patients who was placed in this group was only 6.5 cm. from the midsternum.

We believe that T-wave changes in the absence of coronary heart disease are dependent mainly upon four variables, at least two of which interfere with the normal function of the heart, including conduction: (1) dilatation, (2) hypertrophy or increased muscle mass without compensatory increase in the vascular bed, (3) increased work with subsequent rise in myocardial metabolism, and (4) rotation of the heart on its longitudinal or transverse axis. Slight to moderate changes in heart rate affect the T waves only a little but marked changes in rate, such as that which occurs in paroxysmal tachycardia, may alter them considerably, causing their depression during faster rates.

That T-wave changes are not necessarily due to coronary heart disease is partially confirmed by the fact that when the heart is relieved of "strain" by a decrease in the blood pressure, such as frequently happens following sympathectomy, the T waves may return to normal. The "strain" on the heart is relieved so that myocardial metabolism is lowered and dilatation is lessened. Probably the position of the heart is also altered to some extent.

Other investigators have commented on the lack of definite positive correlation between the heart size and the electrocardiographic changes.[7, 8, 12, 13] Our data showed that the incidence of abnormal electrocardiograms was slightly greater in the group with enlarged hearts than in the one with hearts of normal size. Schnur[25] found the heart to be enlarged in every case in his series in which the T wave was inverted in Lead II, but it was not uncommon in our series to find inverted T waves in Lead II associated with hearts of normal size by teleroentgenogram (39.4 per cent of the patients with inverted T waves in Lead II had hearts of normal size). It is, however, difficult or impossible to recognize slight, or indeed even moderate, cardiac enlargement in many cases by roentgen-ray examination, particularly when there is very little dilatation; it is quite possible that in some cases, at least, the electrocardiogram is a more sensitive index of enlargement of the heart than is the roentgenogram.

A trend toward a positive correlation between the electrocardiographic changes and the degree of retinal changes was noted by Roesler and co-workers.[12] In our series, the electrocardiogram tended to become more abnormal as the eye grounds became worse.

The diastolic pressure on admission to the hospital is notoriously an inaccurate measurement of the individual's usual blood pressure, since it depends so much on many variables, such as the general condition of the patient, the attitude and acuity of hearing of the examiner, and the position of the patient. However, it does give some information as to what height the blood pressure may rise, hence it was correlated with electrocardiographic changes in our cases. No definite positive correlations could be found between the two.

Almost the same statement is true with respect to the correlation between the known duration of the hypertension and electrocardiographic findings. It is a well-known fact that the stated duration of hypertension is a poor estimate of the actual duration and gives no information as to the strain on the heart.

Dyspnea and chest pain may be misleading since they can be due to conditions other than myocardial and coronary insufficiency; however, there was a striking correlation between chest pain and changes in the electrocardiogram. Of the twelve patients who complained of chest pain, all but one had abnormal T waves in Lead I. Peculiarly, there were no abnormal Q waves, conduction defects, or abnormal T waves in Leads II and III among these cases.

SUMMARY AND CONCLUSIONS (A. THE LIMB LEADS)

1. Two hundred nine consecutive patients, upon whom dorsolumbar sympathectomies were performed by R. H. Smithwick at the Massachusetts General Hospital, were selected for study. One hundred fifty electrocardiograms on 132 patients were suitable for analysis. The patients' ages varied from 22 to 58 years, with an average age of 40 years. The known duration of hypertension ranged from two months to twenty-four years. Eye grounds and renal biopsies varied from normal to Grade 4. Hearts were normal to large by teleroentgenogram. The diastolic blood pressure on admission varied from 88 to 180 mm. of mercury.

2. Correlations were made between electrocardiographic changes in the limb leads and (a) the known duration of hypertension, (b) the height of the diastolic pressure on admission, (c) the heart size by teleroentgenogram, (d) symptoms (chest pain and dyspnea), (e) eye-ground findings, and (f) pathologic changes in the kidneys found in biopsy material.

3. Gross analysis of the electrocardiograms revealed that 34.7 per cent were within the range of normal, 27.3 per cent showed abnormal T waves only (less than 1 mm. in height in Lead I), 16 per cent showed left axis deviation only (zero or minus according to Einthoven's triangle), and 22 per cent showed left axis deviation plus abnormal T waves.

4. Early electrocardiographic changes consisted of depression of the RS-T junction and segment in Lead I, lowering of the T wave in Lead I, and lengthening of the QT interval.

5. Axis changes occurred simultaneously with T-wave changes in Lead I but were variable. Sometimes considerable axis change occurred while only slight T-wave alterations appeared and vice versa.

6. Concomitant with changes in the T-wave in Lead I, the most frequent change in Lead III was an elevation of the RS-T segment.

7. Many times the relative changes in Lead III were slight and sometimes the RS-T segment in Lead III, as well as that in Lead I, was depressed.

8. In the electrocardiograms in which the T waves were normally inverted in Lead III, inversion of the T waves first appeared in Leads II and III and later in Leads I, II, and III when there was considerable change in Lead I with only slight change in Lead III or when the RS-T segment was depressed in Lead III as well as Lead I.

9. In the electrocardiograms in which the T waves in Lead III were normally inverted, coronary type T waves appeared in the cases in which the last portion of the RS-T segment and the first portion of the T wave became elevated.

10. Changes in the RS-T segments in Leads II and III are important since they have not been stressed and they frequently have been misinterpreted as changes due to coronary disease.

11. Electrocardiograms tended to become more abnormal as eye-ground changes became worse.

12. There was no definite positive correlation between changes in the electrocardiogram and those in the renal biopsy material; however, the incidence of abnormal electrocardiograms was distinctly greater in the group with Grade 4 renal biopsies than in the other groups.

13. The incidence of abnormal electrocardiograms was only slightly greater in the group with obviously enlarged hearts by roentgen-ray examination than in the one with "normal" sized hearts.

14. The T wave in Lead II may be inverted in hearts of "normal" size.

15. By the time patients complained of pain in the chest, the T waves in Lead I had become abnormal in 91.7 per cent.

16. No positive correlation appeared between dyspnea and electrocardiographic changes.

17. No definite positive correlation was found between electrocardiographic alterations and the known duration of hypertension or the diastolic blood pressure on admission to the hospital.

B. The Precordial Leads

Smithwick's preoperative studies have provided us with excellent material for the analysis of the precordial leads in hypertension. We have been taking precordial Leads CF_2, CF_4, and CF_5 routinely, according to the standards established by the American Heart Association, on all hypertensive patients who are seen for consideration of lumbodorsal sympathectomy. The CF leads are those in which the precordial electrode is paired with an indifferent electrode attached to the left leg, and the positions on the chest are as follows: in taking Lead CF_2, the precordial electrode is placed in the fourth intercostal space just to the left of the sternum; in taking Lead CF_4 it is placed in the fifth intercostal space at the midclavicular line; and in taking Lead CF_5 it is placed in the fifth intercostal space at the anterior axillary line (or in the sixth space if the cardiac apex is located in that space). These three precordial leads have been selected for routine use at the Massachusetts General Hospital because they have been found clinically useful and practicable more often than other combinations.

The present study includes one hundred such electrocardiograms of one hundred cases, for the most part taken consecutively except for the omission of those cases in which digitalis had been given. The ages of the patients varied from 17 to 66 years, averaging 42.4 years, with the distribution of age groups as follows: 45 per cent between 40 and 50 years; 22 per cent between 30 and 40 years; 19 per cent between 50 and 60 years; 9 per cent between 20 and 30 years; 3 per cent between 60 and 70 years; and 2 per cent under 20 years. This group is probably quite representative of hypertensive patients, but it must be remembered that they are somewhat selected patients since a great deal of work was often done before admission to determine whether they were suitable candidates for operation.

The duration of hypertension was known with reasonable certainty in only seventy-three of the one hundred cases. In these it had been present for from four months to twenty years with an average duration of 5.6 years. The systolic and diastolic pressures of the individual patients varied so widely that an accurate average was difficult to obtain. In some cases only one or two admission readings were available; in other cases an average of several readings, some of which were taken after the patient had been at rest in bed for several days, often failed to indicate the severity of the hypertension. However, taking the best average reading obtainable for each patient, we found the diastolic blood pressure 100 mm. or more in ninety-seven cases and

TABLE XII. AMPLITUDE AND DIRECTIONS OF ELECTROCARDIOGRAPHIC COMPLEXES IN HYPERTENSION AS COMPARED WITH THE NORMAL

	R WAVE		S WAVE		T WAVE		DEVIATION OF S-T SEGMENT FROM P-R						
	DIRECTION OF DEFLECTION	AV. AMPLITUDE IN MM.	DIRECTION OF DEFLECTION	AV. AMPLITUDE IN MM.	DIRECTION OF DEFLECTION	AV. AMPLITUDE IN MM.	DIRECTION OF DEFLECTION	AV. DEVIATION IN MM.	MAXIMAL R	MINIMAL R	MAXIMAL S	MINIMAL S	MAXIMAL T	MINIMAL T
CF_2														
10 Normal Adults (Deeds and Barnes)	+10	+6.4	−10	−23.7	+10	+6	+10	+1.9						
50 Normal Males (Deeds and Barnes)	+50	+8.4	−50	−25.4	+50	+7.1	+50	+1.9	16.8	1.1	35	7	+15.5	+3.1
50 Normal Females (Deeds and Barnes)	+50	+4.6	−50	−24.5	+49 0 diphasic 1	+4.3	+49 level 1	+1.3	10.7	0.2	35	12	+10.1	+1.7
100 Normal Persons (Shanno)	+100	+4-7		−19-−22	+94 −6	1-4	+77		13	1	31	9	+7	−2
Our 100 Hypertensive Patients	+100	+4.1	−100	−20.6	+98 −2	5.02	level 23	0.5-3.5	Not known	0-1	Not known	0-1	+11	0
IVF (OR CF_4)														
10 Normal Adults (Deeds and Barnes)	+10	+7.5	−10	−13.1	+10	+5.9	+10	+1.9						
50 Normal Males (Deeds and Barnes)	+50	+11.8	−50	−14.5	+50	+7	+49 −1	+1.3 −0.2	30.8	2.8	35	1.4	+14.3	+0.8
50 Normal Females (Deeds and Barnes)	+50	+7.5	−50	−14.3	+50	+5.4	+48 level 2	+1.0	39	1.2	27.3	2.2	+9.3	+1.3
100 Normal Persons (Shanno)		+4-8		−0-23		2-4			14	1	19	0	+7	−1
Our 100 Hypertensive Patients (Lead CF_4)		+14.8		−9.3	−20 diphasic 2 +78	3.84	−15 level 85	0.5-1.5	Not known	6	Not known	1	+8	+0-1
CF_5														
10 Normal Adults (Deeds and Barnes)	+10	+19.3	−10	−7.0	+10	+4.8	+8 −2	+0.7 −0.4						
50 Normal Males (Deeds and Barnes)	+50	+16.4	−50	−7.4	+50	+5.4	+40 −2 level 8	+0.7 −0.7	35	4.7	22	1.8	+12.0	+0.7
50 Normal Females (Deeds and Barnes)	+50	+12	−46 +4	−5.8	+50	+4.7	+33 −6 level 11	+0.5 −0.3	24.9	1.8	18.7	8.6	+8.9	+1.2
100 Normal Persons (Shanno)		+4-8		−0-23		1-4			20	2	12	0	+6	+8
Our 100 Hypertensive Patients		+15.2		−2.3	diphasic 2 −33 +65	2.25	−21 level 79	−0.5 to −2.5	Not known	5.5	11	0	+4	+0

the systolic pressure 160 mm. or more in ninety-eight cases, the upper limits being 270 systolic and 160 diastolic. Eye-ground changes and renal biopsies varied from normal to Grade 4 according to the system of grading described previously in this paper. Heart size as determined by x-ray examination ranged from normal through hearts which had a slightly prominent or rounded ventricle to hearts which showed definite enlargement by measurement.

The work of Deeds and Barnes[26] who studied the precordial leads in 110 normal adults between the ages of 21 and 33 years and that of Shanno[27] who analyzed them in one hundred normal student nurses have been utilized to give some control standards for comparison, and their average values are recorded with ours in Table XII. Their IVF lead is not always comparable to our Lead CF_4 but was included since a great number of the hearts in our series were not enlarged, and Lead IVF and Lead CF_4 would then coincide.

QRS WAVES IN THE PRECORDIAL LEADS OF THE ENTIRE SERIES

In our series of one hundred cases the voltage of the QRS complexes varied a great deal, and an accurate average was impossible to obtain because the string went off the film often when the voltage was high. However, when exact measurements were possible, as they were in the great majority of cases, the average height of the R wave in Lead CF_2 was 4.1 mm., in Lead CF_4 14.8 mm., and in Lead CF_5 15.2 millimeters. In four cases the R wave was absent in Lead CF_2, and in one case it was absent in Leads CF_2, CF_4, and CF_5 so that the tracing suggested the presence of an old anterior myocardial infarction although there was no history of one. These figures can be compared with those of Deeds and Barnes[26] whose findings were as follows: the average amplitude of the R wave in Lead CF_2 was 8.4 mm. in males and 4.6 mm. in females; in Lead IVF it was 11.8 mm. in males and 7.5 mm. in females; and in Lead CF_5 it was 16.4 mm. in males and 12 mm. in females. In Shanno's series[27] it was 4 to 7 mm. in Lead CF_2, 4 to 8 mm. in Lead IVF, and slightly more than the average of Lead IVF in Lead CF_5. The average amplitude of the S wave in our series was 20.6 mm. in Lead CF_2, 9.3 mm. in Lead CF_4 and 2.3 mm. in Lead CF_5. These findings can be compared with those of Deeds and Barnes and of Shanno which were as follows: Deeds and Barnes gave the average amplitude of the S wave in Lead CF_2 as 25.4 mm. in males and 24.5 mm. in females, in Lead IVF as 14.5 mm. in both males and females, and in Lead CF_5 as 7 mm. in males and 7.4 mm. in females; Shanno obtained an average amplitude of 19 to 22 mm. in Lead CF_2, 0 to 23 mm. in Lead IVF, and slightly less than that in Lead CF_5.

We considered any voltage of the R wave or the S wave of 25 mm. as borderline, and any of 25 to 30 mm. or over as high. The duration of the QRS complexes varied from 0.07 to 0.11 second with the greatest number measuring 0.08 second.

The RS-T segment in Lead CF_2 was elevated in seventy-seven instances; the deviation from the base line varied from 0.5 to 3.5 millimeters. The RS-T segment in Lead CF_4 was elevated only fifteen times, the deviation varying from 0.5 to 1.5 millimeters. The RS-T segment in Lead CF_5 was depressed from 0.5 to 2.5 mm. in twenty-one instances.

T WAVES IN THE ENTIRE SERIES

The average height of the T waves in Lead CF_2 was 5.02 millimeters. This figure is very close to the average amplitude of the normals of Deeds and

Barnes who found it 4.3 mm. in females and of Shanno who found it from 1 to 4 millimeters. However, the average amplitude of the T waves in Lead CF_2 in Deeds and Barnes' series of 50 males was 7.1 mm., the maximal T wave being 15.5 mm. and the minimal T wave 3 mm. The highest in our series was 11 mm., and it seemed to us from our study that any T wave 7 mm. or more in amplitude might be called relatively high. The lowest T wave in Lead CF_2 in our series was 1 mm. in height.

The average amplitude of the positive T waves in Lead CF_4 was 3.84 millimeters. This average is in accord with the average of 2 to 4 mm. which Shanno found in Lead IVF but lower than the 7 mm. in fifty males and the 5.4 mm. in fifty females which Deeds and Barnes found. The highest in our series was 8 mm. as compared to a maximal T wave of 14.3 mm. in Deeds and Barnes' series of fifty males, 9.3 mm. in their series of fifty females, and 7 mm. in Shanno's series. In this lead also we recorded any T wave which was 7 mm. or more in amplitude as relatively high.

The average amplitude of the positive T waves in Lead CF_5 was 2.25 millimeters. This average is again in agreement with the findings of Shanno who gives the average amplitude in this lead as 1 to 4 mm.; and again the figures of Deeds and Barnes are higher, being 5.4 and 4.7 mm. for males and females, respectively, with maximal T waves of 12 and 8.9 millimeters. The highest T wave in our series was 4 mm., and again the figures of Deeds and Barnes are higher, being 5.4 and 4.7 mm. for males and females, respectively, with maximal T waves of 12 and 8.9 millimeters. We considered any T wave which was only 1 mm. in amplitude as borderline and any which was less than 1 mm. definitely abnormal.

NORMAL T WAVES

Fifty of our one hundred precordial electrocardiograms were within normal limits as to T waves, but because of the presence of some changes which we thought noteworthy we subdivided the group as follows: in thirty-four cases the T waves were normal and the precordial leads probably within normal limits. In twelve cases we found no distinct T-wave abnormalities but noted that the amplitude of the T wave in Lead CF_2 was relatively high, and in four cases there was an unusually high T wave in Leads CF_2 and CF_4. Eight of the cases with no T-wave changes, four of the twelve cases showing relatively high T waves in Lead CF_2, and three of the four cases showing relatively high T waves in both Leads CF_2 and CF_4 had in addition rather high voltage of the QRS complexes in one or more of the three precordial leads.

Forty-one of the fifty cases with normal precordial leads also showed normal limb leads except for left axis deviation which appeared in twenty-one cases. Subdividing these as we have already mentioned we found the following: in twenty-nine of the thirty-four cases showing normal precordial leads as to T waves, the limb leads were normal except for left axis deviation which occurred in seventeen cases; ten of the twelve cases showing unusually high T waves in Lead CF_2 had normal limb leads except for left axis deviation in three, and two of the four cases showing unusually high T waves in Leads CF_2 and CF_4 had normal limb leads except for left axis deviation in one. In Fig. 1 there is an electrocardiogram representative of this group of normal precordial leads in hypertensive patients; it shows no T-wave abnormalities.

ABNORMAL T WAVES

In fifty of our one hundred cases we found some definite abnormalities in the precordial T waves. In thirteen cases T-wave changes (including low T in eight, diphasic T in one, and inverted T in four cases) occurred only in Lead CF_5; in three of these cases there was also unusually high voltage of the QRS complexes in one or more leads. In ten cases there were T-wave changes in both Lead CF_2 and Lead CF_5 as follows: very high T in Lead CF_2 with low T in Lead CF_5 in three cases; very high T in Lead CF_2 with inverted T in Lead CF_5 in six cases; and a low T wave in Lead CF_2 with an inverted T wave in Lead CF_5 in one case. In one instance there was a rather high T wave in Lead CF_4 with a low T wave in Lead CF_5, and in one there was a relatively high

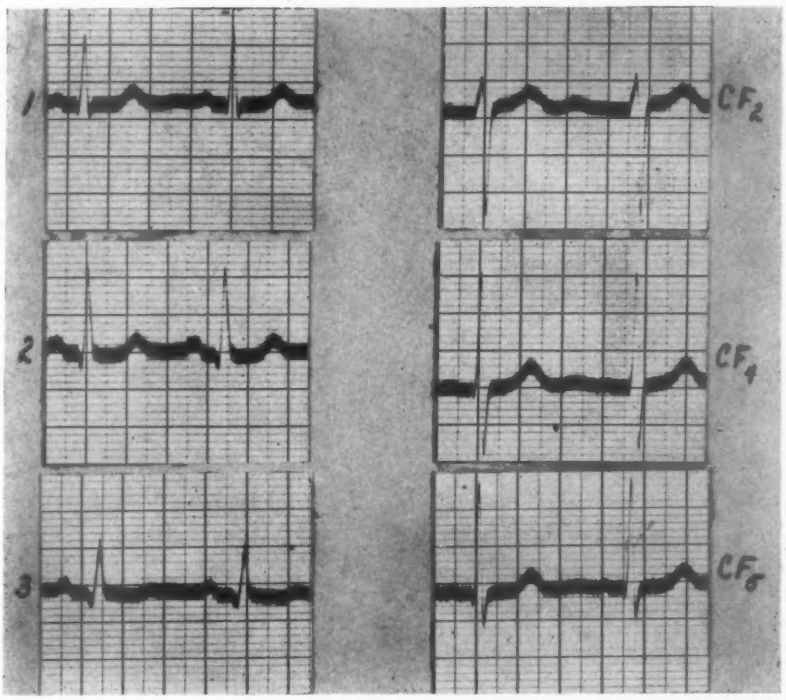

Fig. 1.—H. V., a woman, aged 52 years. Electrocardiogram taken March 22, 1944; blood pressure, 200/100. Normal record (both limb and precordial leads).

T wave in Leads CF_2 and CF_4 with borderline low T in Lead CF_5. Thus, there were important T-wave changes in Lead CF_5 in twenty-five of our fifty abnormal precordial leads, and in seventeen of these twenty-five the limb leads were also abnormal. In fact, as was to be expected, the T wave in Lead CF_5 often resembled that in Lead I. Figs. 3, 4, and 5 show electrocardiograms which are characteristic of some of the ones seen in this group; the T wave in Lead CF_5 is inverted.

In fifteen of the one hundred cases there were changes in the T waves in both Leads CF_4 and CF_5 as follows: inverted T in Leads CF_4 and CF_5 in eleven cases; low T in Lead CF_4 and inverted T in Lead CF_5 in two cases; and inverted T in Lead CF_4 and low T in Lead CF_5 in two cases. In thirteen of these fifteen cases the limb leads were abnormal. In ten cases there were changes in Lead CF_2 in addition to the abnormalities of the T waves in Leads

CF_4 and CF_5 as follows: four cases showed very high T waves in Lead CF_2 and inverted T waves in Leads CF_4 and CF_5; one showed low T waves in Leads CF_2, CF_4, and CF_5; three showed very high T waves in Lead CF_2, low or diphasic T waves in Lead CF_4, and inverted T waves in Lead CF_5; and one showed low T waves in Lead CF_2 and inverted T waves in Leads CF_4 and CF_5. Six of the ten cases had, in addition to T-wave abnormalities, very high voltage of the QRS complexes in one or more leads. Nine of the ten had abnormal limb leads, eight with abnormal T_1 and T_2, and one with only a borderline low T_1.

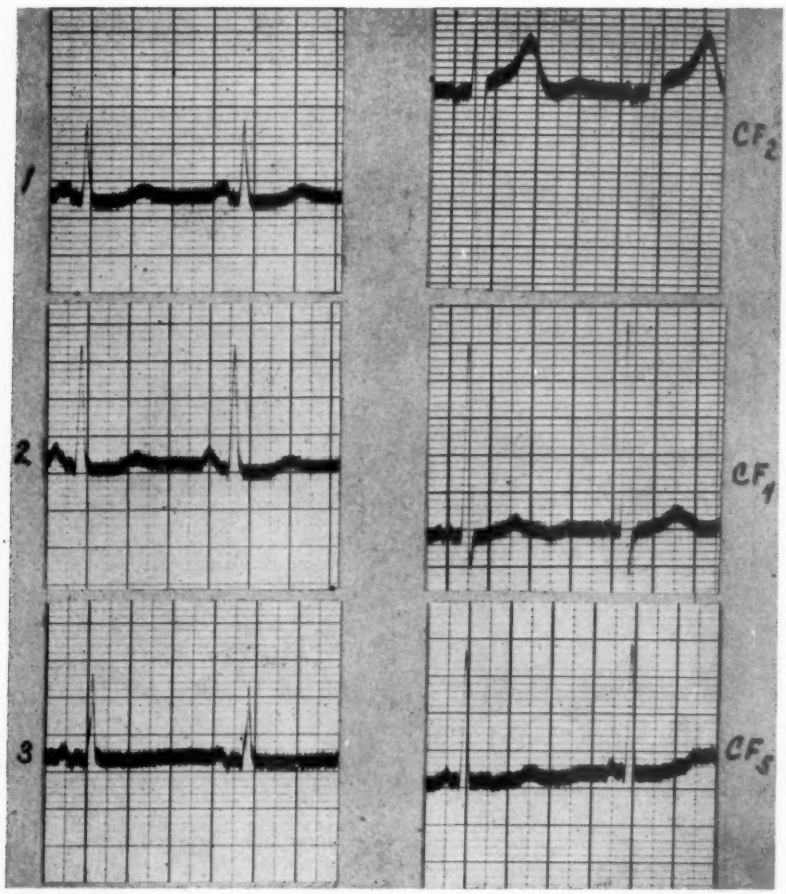

Fig. 2.—M. N., a woman, aged 56 years. Electrocardiogram taken Nov. 27, 1944; blood pressure, 190/110. Electrocardiogram showing slight depression of S-T segments in Lead I and low T waves in the limb leads and in Leads CF_4 and CF_5.

Thus, in twenty-five of our one hundred cases there were important T-wave abnormalities in Leads CF_4 and CF_5. This group is represented by the electrocardiogram shown in Fig. 6 which has inverted T waves in Leads CF_4 and CF_5. In Fig. 5 there is presented a tracing which is characteristic of those seen in moderately advanced hypertensive heart disease and in Fig. 6 a tracing such as is seen in far-advanced cases.

CORRELATIONS

In Table XIII the T-wave changes in the precordial leads are correlated with the height of the diastolic blood pressure. In general it may be said that

TABLE XIII. T-WAVE CHANGES IN THE PRECORDIAL LEADS CORRELATED WITH DIASTOLIC BLOOD PRESSURES

DIASTOLIC B.P.	NUMBER OF ECG'S	NORMAL PRECORDIAL LEADS T-WAVE CHANGES			ABNORMAL PRECORDIAL LEADS T-WAVE CHANGES				TOTAL ABNORMAL
		NONE	IN CF_2	IN CF_2 AND CF_4	IN CF_5	IN CF_4 AND CF_5	IN $CF_{2, 4, 5}$	IN CF_2 AND CF_5	
91-120	47	18 (38.3%)	7 (14.9%)	2 (4.2%)	8 (17%)	6 (12.8%)	4 (8.5%)	2 (4.2%)	20 (42.5%)
121-140	44	15 (34.1%)	3 (6.8%)	1 (2.2%)	7 (15.9%)	11 (25%)	3 (6.8%)	4 (9.1%)	25 (56.8%)
Over 140	9	1 (11.1%)	1 (11.1%)	0 (0%)	0 (0%)	0 (0%)	3 (33.3%)	4 (44.4%)	7 (77.7%)

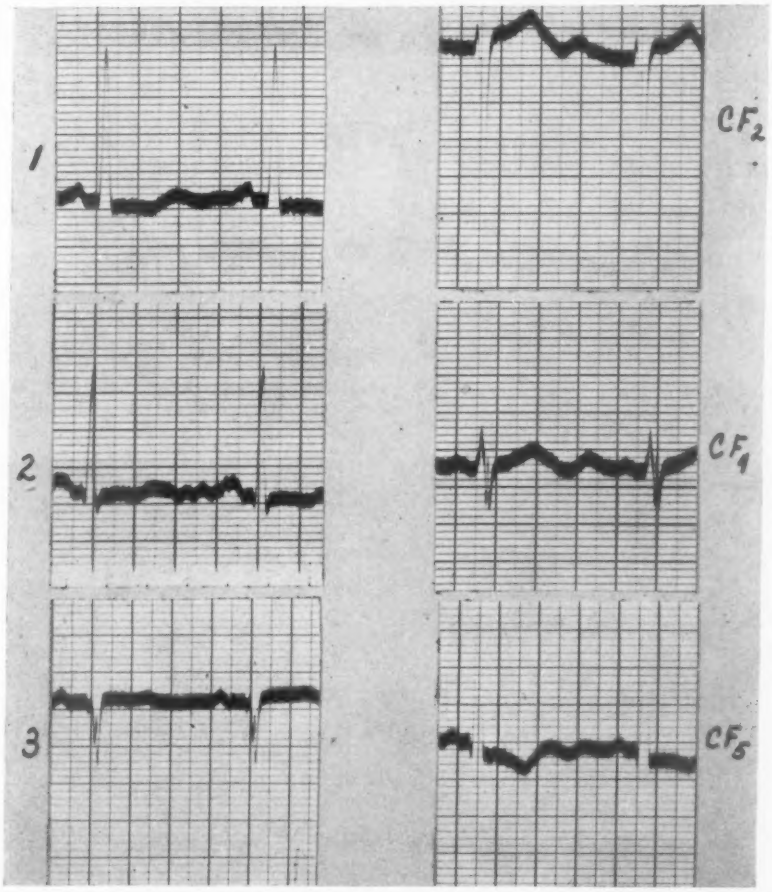

Fig. 3.—M. M., a woman, aged 49 years. Electrocardiogram taken Sept. 29, 1943; blood pressure, 270/122. Hypertensive pattern with depression of S-T segments in Leads I and CF_5, slightly inverted T waves in Leads I, II, and CF_5, prominent U waves in Leads CF_2 and CF_4, and inverted U waves in CF_5.

the percentage of abnormal precordial leads is greater in the groups which have the highest diastolic blood pressures.

In Table XIV the T-wave changes in the precordial leads are correlated with the duration of hypertension. The histories given us as to the duration of hypertension were quite unreliable since it was an accidental and incidental finding in many cases. So it is not surprising that there is little correlation between the electrocardiogram and the known duration of hypertension.

In Table XV the T-wave changes in the precordial leads are correlated with the heart size. Contrary to our findings in the limb leads, a much larger

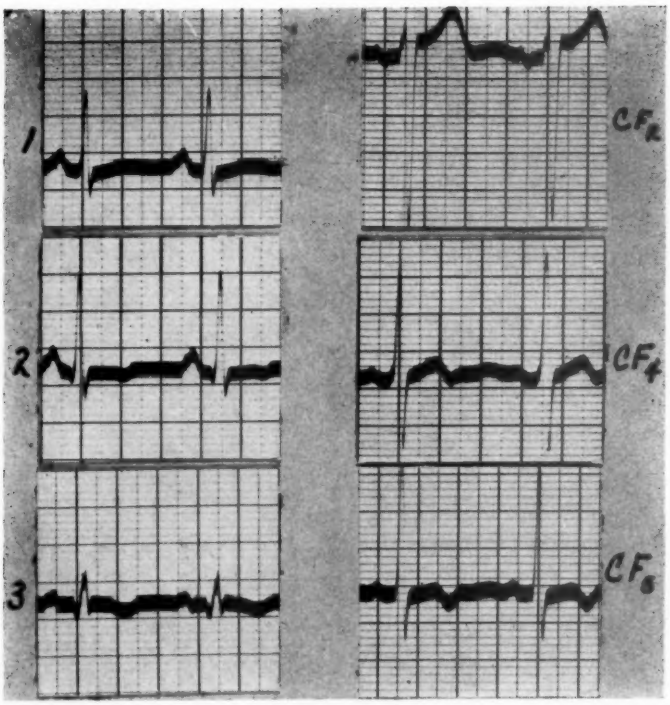

Fig. 4.—F. H., a man, 45 years of age. Electrocardiogram taken June 23, 1944; blood pressure, 190/140. Hypertensive pattern of other type with low T waves in Lead I and inverted T waves in Leads II, III, and CF_5.

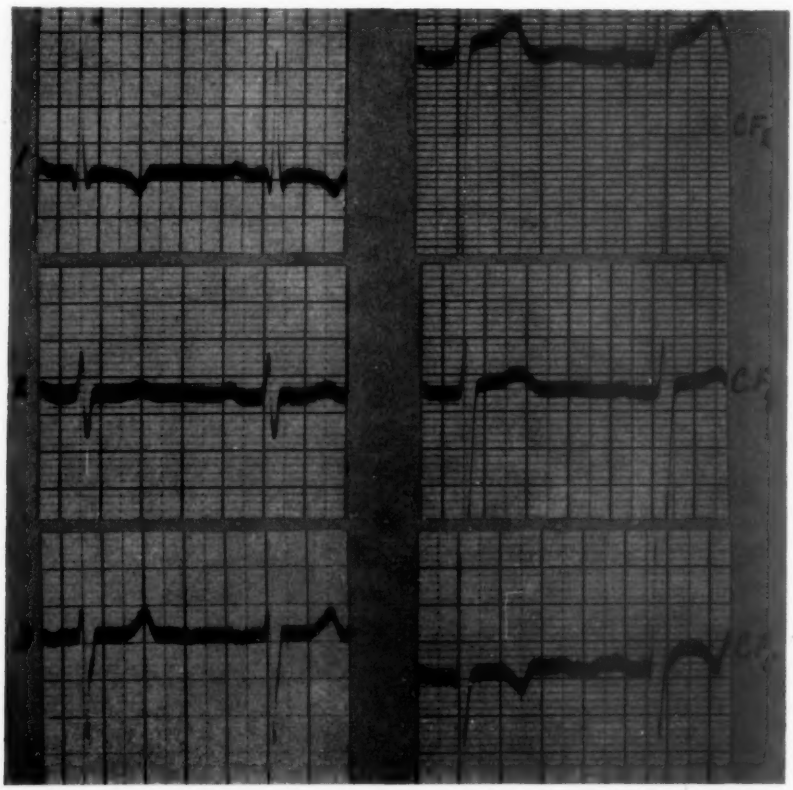

Fig. 5.—E. J., a woman, aged 55 years. Electrocardiogram taken Nov. 28, 1944; blood pressure, 180/110. (Hypertension present for twelve years.) Well-marked hypertensive pattern with considerable left axis deviation and inversion of the T waves in Leads I and CF_5.

TABLE XIV. T-WAVE CHANGES IN THE PRECORDIAL LEADS CORRELATED WITH THE KNOWN DURATION OF HYPERTENSION

DURATION IN YRS.	NUMBER OF ECG'S	NORMAL PRECORDIAL LEADS T-WAVE CHANGES			ABNORMAL PRECORDIAL LEADS T-WAVE CHANGES				TOTAL ABNORMAL PRECORDIAL LEADS
		NONE	IN CF_2	IN $CF_{2,4}$	IN CF_5	IN $CF_{4,5}$	IN $CF_{3,5}$	IN $CF_{2,4,5}$	
1	8	2 (25%)	3 (37.5%)	0	0	3 (37.5%)	0		3 (37.5%)
2	14	6 (42.9%)	2 (14.3%)	0	2 (14.3%)	2 (14.3%)	2 (14.3%)	0	6 (42.9%)
3	8	3 (37.5%)	0	1 (12.5%)	1 (12.5%)	1 (12.5%)	2 (25%)	0	4 (50%)
4	4	2 (50%)	1 (25%)	0	1 (25%)	0	0	0	1 (25%)
5	7	3 (42.9%)	1 (14.3%)	0	1 (14.3%)	1 (14.3%)	1 (14.3%)	0	3 (42.9%)
10	21	6 (28.6%)	3 (14.3%)	1 (4.8%)	3 (14.3%)	5 (23.9%)	1 (4.8%)	2 (9.5%)	11 (52.4%)
15	9	2 (22.2%)	1 (11.1%)	0	0	3 (33.3%)	1 (11.1%)	2 (22.2%)	6 (66.6%)
20	3	1 (33.3%)					1 (33.3%)	1 (33.3%)	2 (66.6%)
25	1	0			1 (100%)				1 (100%)

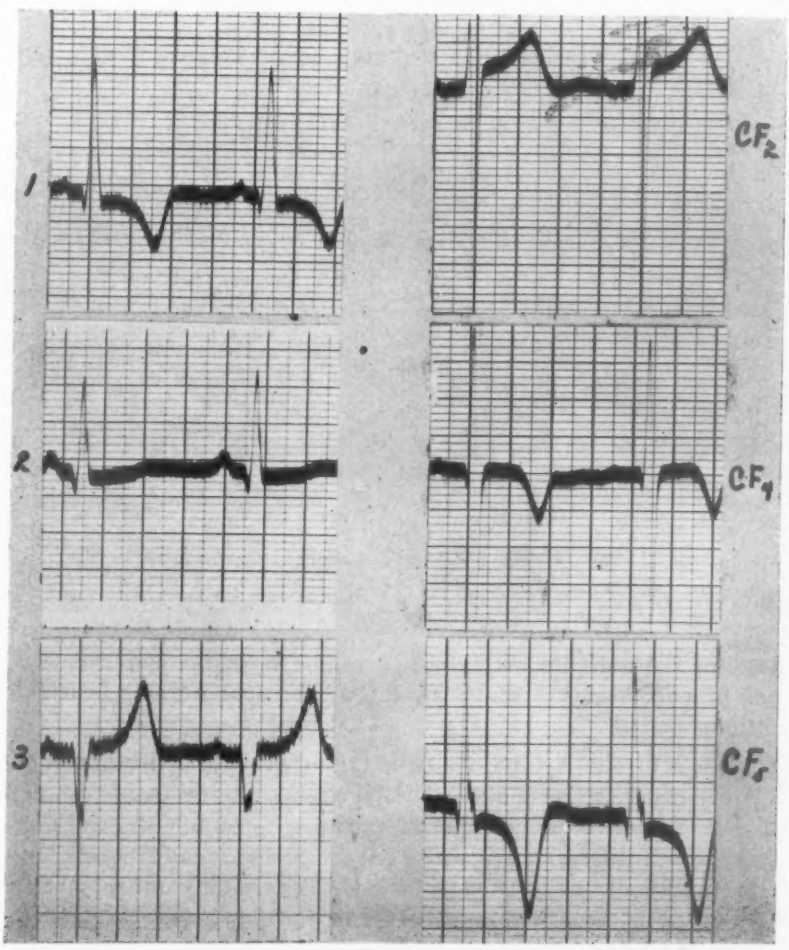

Fig. 6.—N. T., a man, aged 52 years. Electrocardiogram taken Nov. 22, 1944; blood pressure, 208/110. Marked hypertensive pattern with slight left axis deviation, depressed S-T segments in Leads I and CF_5, and deep inversion of the T waves in Leads I, CF_4 and CF_5.

TABLE XV. CORRELATION OF T-WAVE CHANGES IN THE PRECORDIAL LEADS WITH THE HEART SIZE

SIZE	NUMBER OF ECG'S	NORMAL PRECORDIAL LEADS T-WAVE CHANGES			ABNORMAL PRECORDIAL LEADS T-WAVE CHANGES				TOTAL ABNORMAL
		NONE	IN CF_2	IN $CF_{2,4}$	IN CF_5	IN $CF_{2,5}$	IN $CF_{4,5}$	IN $CF_{2,4,5}$	
Normal	28	18 (64.3%)	2 (7.1%)	1 (3.6%)	6 (21.4%)	0	1 (3.6%)	0	7 (25%)
Prominence of left ventricle or rounded apex	41	9 (22%)	6 (14.6%)	1 (2.4%)	8 (19.5%)	6 (14.6%)	9 (22%)	2 (4.9%)	25 (60.9%)
Enlarged	20	5 (25%)	2 (10%)	0	1 (5%)	3 (15%)	4 (20%)	5 (25%)	13 (65%)

TABLE XVI. CORRELATION OF T-WAVE CHANGES IN PRECORDIAL LEADS WITH EYE-GROUND CLASSIFICATION

EYE GROUNDS	NUMBER OF ECG'S	NORMAL PRECORDIAL LEADS T-WAVE CHANGES			ABNORMAL PRECORDIAL LEADS T-WAVE CHANGES				TOTAL ABNORMAL LEADS
		NONE	IN CF_2	IN $CF_{2,4}$	IN CF_5	IN $CF_{2,5}$	IN $CF_{4,5}$	IN $CF_{2,4,5}$	
N	15	8 (53.3%)	1 (6.7%)	0	2 (13.3%)	0	3 (20.0%)	1 (6.7%)	6 (40.0%)
1	27	8 (29.6%)	6 (22.2%)	0	2 (7.4%)	5 (18.5%)	6 (22.2%)	0	13 (48.1%)
2	26	5 (19.2%)	1 (3.8%)	2 (7.7%)	3 (11.5%)	4 (15.4%)	9 (34.6%)	2 (7.7%)	18 (69.2%)
3	10	6 (60%)	1 (10%)	1 (10%)	1 (10%)	1 (10%)	0	0	2 (20%)
4	4	0	0	0	2 (50%)		1 (25%)	1 (25%)	4 (100%)

TABLE XVII. CORRELATION OF T-WAVE CHANGES IN THE PRECORDIAL LEADS WITH RENAL BIOPSIES

RENAL BIOPSY GRADE	NUMBER OF ECG'S	NORMAL PRECORDIAL LEADS T-WAVE CHANGES			ABNORMAL PRECORDIAL LEADS T-WAVE CHANGES				TOTAL ABNORMAL
		NONE	IN CF_2	IN $CF_{2,4}$	IN CF_5	IN $CF_{2,5}$	IN $CF_{4,5}$	IN $CF_{2,4,5}$	
0	1	1 (100%)							0 (0%)
1	4	3 (75%)					1 (25%)		1 (25%)
2	4	1 (25%)	1 (25%)		1 (25%)		1 (25%)		2 (50%)
3	16	6 (37.5%)	2 (12.5%)		2 (12.5%)	3 (18.8%)	3 (18.8%)		8 (50%)
4	1	1 (100%)							

percentage of the patients with slight or definite cardiac enlargement showed abnormal precordial leads than did those who had normal hearts by x-ray examination.

In Table XVI the T-wave changes in the precordial leads are correlated with the eye-ground classification. In general an increasing percentage of precordial leads showed abnormalities as the eye grounds showed more pathologic changes. However, there was a larger percentage of normal tracings in the group that had Grade 3 eye grounds than in any other; that is to be accounted for, doubtless by the smallness of the numbers.

In Table XVII the T-wave changes in the precordial leads are correlated with renal biopsies. We had only one patient with a Grade 4 renal biopsy who showed a normal electrocardiographic tracing. Except for that discrepancy,

a greater percentage of the precordial leads were abnormal in the cases which showed Grade 2 and 3 pathologic change than in those which showed Grade 0 to 1. The percentage of abnormal tracings was the same in the patients showing Grades 2 and 3 pathologic findings, however. These figures are not reliable since the number of renal biopsies was small.[25]

In Table XVIII the precordial and limb leads are correlated. When the precordial leads were normal the limb leads were normal in 82 per cent of the cases and abnormal in 18 per cent of the cases. When the precordial leads were abnormal, the limb leads were abnormal in 78 per cent of the cases and normal in 22 per cent of the cases.

TABLE XVIII. CORRELATION OF NORMAL AND ABNORMAL PRECORDIAL LEADS WITH NORMAL AND ABNORMAL LIMB LEADS

PRECORDIAL LEADS	NUMBER OF ECG'S	NORMAL LIMB LEADS	ABNORMAL LIMB LEADS
Normal	50	41 (82%)	9 (18%)
Abnormal	50	11 (22%)	39 (78%)
LIMB LEADS	**NUMBER OF ECG'S**	**NORMAL PRECORDIAL LEADS**	**ABNORMAL PRECORDIAL LEADS**
Normal	52	41 (78.8%)	11 (21.1%)
Abnormal	48	9 (18.7%)	39 (81.3%)

Table XIX presents a correlation between the amplitude of the QRS waves and abnormalities of the T waves of the precordial electrocardiograms. There is evidently a connection between high voltage of the QRS waves in Leads CF_4 and CF_5 and abnormalities (commonly inversion) of the T waves in these same leads.

TABLE XIX. CORRELATION OF AMPLITUDE OF QRS WAVES AND OF T-WAVE ABNORMALITIES IN HYPERTENSIVE ELECTROCARDIOGRAMS

	NUMBER	NO T-WAVE CHANGES	ABNORMAL T WAVES			
			IN CF_5 ALONE	IN LEADS CF_4 AND CF_5	IN LEADS CF_3, CF_4, AND CF_5	TOTAL NUMBER
High voltage of QRS in Leads CF_3, CF_4, and CF_5	15	3 (20%)	4 (26.7%)	7 (46.6%)	1 (6.7%)	12 (80%)
High voltage in CF_3	16	10	3	3	0	6 (37.5%)
In CF_4 and CF_5	5	1	1	3	0	4 (80%)
In CF_4 only	2	0	1	1	0	2
In CF_3 and CF_4	2	2	0	0	0	0
Total	40	16	9	14	1	24

DISCUSSION

In general this study has shown that low, diphasic, or inverted T waves in Leads CF_4 and CF_5 are consistent with hypertensive heart disease. In addition, as we have indicated, high voltage of the QRS complexes in one or more of the precordial leads is a rather common finding and one to be expected, according to the work of Wilson,[28] in cases with left ventricular hypertrophy: "In left ventricular hypertrophy the voltage of the chief deflection of the QRS group is on the average much greater than normal, and the QRS interval is increased to 0.10 or even 0.11 second. In the leads from the right side of the precordium the R deflections are, on the average, much smaller than normal and may be absent. The transitional zone is, as a rule, much displaced to the

left. In the leads from the left side of the precordium R and often Q as well, are abnormally large; the peak of R occurs abnormally late in the QRS interval; and the T deflections are inverted." Changes in the QRS complexes in our series, aside from these changes in voltage and absent R waves in the five cases mentioned, were not outstanding. A few were notched or slurred and an occasional one was w-shaped; there was no particular widening although a few measured 0.10 to 0.11 second.

The changes in the T wave in Lead CF_2 are interesting but their significance is not clear. Low or inverted T waves in Lead CF_2 may rarely occur in normal tracings and are not necessarily an abnormal finding. The relatively high T wave seen rather frequently in this lead may perhaps be a characteristic finding in hypertensive heart disease; there is no reason to believe that it is an abnormal finding, however, and it is certainly not specific since it is seen in posterior myocardial infarction and even in normal persons. It is necessary to remember that we do not as yet have enough normal controls to know what the range of the normal amplitude of the T wave in Lead CF_2 is. There is similar uncertainty about the significance of the relatively high T wave in Lead CF_4; it may also occur in normal tracings and in those showing evidence of posterior myocardial infarction. Thus, again in this case, we do not know well enough the range of the normal or even the average. Elevation of the RS-T segment in Lead CF_2 of from 0.5 to 2 mm. occurs too frequently normally to be significant in our series. RS-T segment changes in Lead CF_4 were rare and not in themselves significant. Depression of the RS-T segment in Lead CF_5 appeared rather frequently, usually together with an inverted or diphasic T wave.

In correlating changes in the precordial leads with those in limb leads we found that they were usually similar, both being normal or both being abnormal in the greatest percentage of cases. In forty-one of our one hundred electrocardiograms both precordial and limb leads were within normal limits; in thirty-nine cases both showed some abnormality. Abnormal limb leads were accompanied by normal precordial leads in only nine cases, while abnormal precordial leads were accompanied by normal limb leads in eleven cases. The T waves in Lead CF_4 and CF_5 often showed abnormalities similar to those of the T waves in Leads I and II, thus supporting and confirming the evidence of cardiac involvement provided by the limb leads. Sometimes a tracing which had a borderline or questionably low T wave in Lead I and which would have to be considered within normal limits so far as the limb leads are concerned showed abnormalities in the precordial leads which make it consistent with hypertensive heart disease and lend significance to the minimal changes in the limb leads. It is true that the T-wave changes cannot be considered diagnostic since they are similar to those in coronary heart disease. However, as was mentioned in the discussion of changes in the limb leads, the early age at which the T waves become low or deeply inverted in the hypertensive patients, the fact that a number of them do revert to normal after lumbodorsal sympathectomy, and the absence of the pain of coronary insufficiency tend to rule out coronary heart disease in most instances. With the return of low and inverted T waves to normal voltage it becomes evident that the changes in many tracings which we read as consistent with hypertensive and/or coronary heart disease are to be ascribed as a rule alone to hypertensive heart disease.

From the data obtained in our study it is evident that the first changes due to hypertensive heart disease appear in the electrocardiogram in either

the limb leads or the precordial leads or both. We cannot yet determine their relative importance. However, it is clear that the changes in the precordial leads are at least as characteristic as are those in the limb leads, and we can conclude, therefore, that precordial lead electrocardiographic changes are as important and helpful in the detection of hypertensive heart disease as are changes in the limb leads, and perhaps more so.

SUMMARY AND CONCLUSIONS (B. THE PRECORDIAL LEADS)

1. Precordial Leads CF_2, CF_4, and CF_5 have been analyzed in the electrocardiograms of one hundred hypertensive patients upon whom preoperative studies for the Smithwick lumbodorsal sympathectomy were being done. The ages varied from 17 to 66 years with an average age of 42.4 years. The blood pressure readings ranged from 270 to 150 systolic and from 160 to 95 diastolic.

2. The precordial leads were normal as to T waves in fifty of the one hundred cases, but due to the presence of certain changes which were considered worthy of note, these fifty were subdivided as follows: in thirty-four cases they were well within the usual normal limits; in twelve cases there were unusually high T waves in Lead CF_2; and in four cases there were unusually high T waves in Leads CF_2 and CF_4.

3. The QRS waves in general showed no striking abnormalities; however, R waves were absent in Lead CF_2 in four cases and in Leads CF_2, CF_4, and CF_5 in one case, the voltage of the R or S waves was relatively high in one or more of the three precordial leads in twenty-four cases, and there was a definite correlation between high voltage of the QRS waves and abnormalities of the T waves in Leads CF_4 and CF_5. The R and S waves were not unusually low in any of the electrocardiograms in this series.

4. The precordial leads showed definite abnormalities of the T waves in fifty of our one hundred cases, twenty-five showing abnormal T waves in Lead CF_5, and twenty-five showing abnormal T waves in both Leads CF_4 and CF_5 as follows: in thirteen cases T wave changes occurred only in Lead CF_5; in eleven cases there were changes in both Leads CF_2 and CF_5; in one case there were rather high T waves in Lead CF_4 with a low T wave in Lead CF_5; in eleven cases there were inverted T waves in Leads CF_4 and CF_5; in two cases there were low T waves in Lead CF_4 and inverted T waves in Lead CF_5; in two cases there were inverted T waves in Lead CF_4 and low T waves in Lead CF_5; in ten cases there were abnormalities of the T waves in Lead CF_2 as well as in Leads CF_4 and CF_5.

5. Correlations of the T wave changes in the precordial leads with diastolic blood pressures revealed that the percentage of abnormal leads is greatest in the groups which have the highest diastolic pressure. Correlation with the known duration of hypertension was inconclusive and unsatisfactory. Correlation between heart size and the electrocardiographic changes showed a larger percentage of abnormal tracings in the group with slight or considerable cardiac enlargement than in the group with normal-sized hearts. Results from the correlations with the eye-ground changes and the renal biopsy findings were unsatisfactory. When the precordial leads were normal, the limb leads were normal in 82 per cent of the cases and abnormal in 18 per cent of the cases; when the precordial leads were abnormal the limb leads were abnormal in 78.8 per cent of the cases and normal in 21.2 per cent of the cases.

6. In general these studies have shown that low, diphasic, or inverted T waves in Leads CF_4 and CF_5 are commonly found in hypertensive heart disease.

7. In forty-one of our one hundred electrocardiograms both precordial and limb leads were within normal limits; in thirty-nine both showed some abnormality. Abnormal limb leads were accompanied by normal precordial leads in only nine cases while in eleven cases normal limb leads were accompanied by abnormal precordial leads. Hence, in 21 per cent of the cases, precordial leads showed abnormalities which would not have been noted if only limb leads had been available.

8. It is evident that the changes in the precordial Leads CF_2, CF_4, and CF_5 in hypertensive heart disease, although not definitely diagnostic, are as characteristic as are those in the limb leads, and we can conclude that they are equally as important and helpful in the detection of changes in hypertensive heart disease as the electrocardiographic changes in the limb leads and may uncover evidence not found in the limb leads alone.

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THE ELECTROCARDIOGRAM IN HYPERTENSION

II. THE EFFECT OF RADICAL LUMBODORSAL SYMPATHECTOMY (PRELIMINARY REPORT)

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IT IS an uncommon clinical experience to encounter patients with well-established hypertension of considerable degree who spontaneously lose their hypertension and the manifestations thereof, including characteristic abnormalities of the electrocardiogram. Over a period of twenty-five years we have faced discouragement as we have followed the generally downward course of the hypertensive cardiac patient. Three years ago a change became clearly apparent, a change that had doubtless already been going on for a few years before that, ever since the introduction of the more extensive lumbodorsal splanchnic sympathectomy for hypertension. Not only was the hypertension being controlled to a greater or lesser degree by this procedure in the majority of the patients, but the secondary cardiac manifestations, especially electrocardiographic, were also sometimes strikingly altered for the better. In other words, there was definite indication at last that, like the thyrocardiac patient of twenty years ago, the hypertensive cardiac patient was becoming amenable to improvement by surgical measures. And so this type of heart disease, too, is, to at least a certain extent, reversible if not allowed to reach an extreme and fixed status.

Improvement in the electrocardiogram following various operations for the relief of hypertension has been mentioned several times[1-5] but none of the reports has given criteria for improvement or adequate control studies, and no correlations were made. Only one gave any statistical data.[4] The newer surgical treatment of hypertension has afforded us this opportunity not only to study postoperative changes in the electrocardiogram but to make numerous correlations between these and other changes concomitant with hypertension, including pathologic changes in the kidney. The paper that follows this will present control studies of the electrocardiogram in hypertension and its more or less natural evolution.

THE OPERATION

Briefly, the operation consists of an extensive bilateral splanchnic denervation, removal of the great splanchnic nerves from the semilunar ganglion to ap-

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proximately the mid-thoracic level, and resection of the sympathetic trunk from the ninth dorsal to the first or second and occasionally the third lumbar ganglion.

MATERIAL

A. *Limb Leads.*—Two hundred nine consecutive patients, upon whom lumbodorsal sympathectomies[6] were performed by R. H. Smithwick at the Massachusetts General Hospital, were selected for study. Eighty-seven postoperative electrocardiograms were compared with the seventy-four records taken before operation on seventy-four patients who showed abnormal tracings to start with; the additional thirteen tracings were follow-up records of several of the seventy-four patients at later dates. The ages varied from 18 to 58 years with an average age of 40.1 years. The known duration of hypertension ranged from two months to twenty-four years. Eye grounds and renal biopsies varied from normal to Grade 4. The diastolic pressure on admission varied from 88 to 170 mm. of mercury. Hearts varied from normal to large by teleroentgenogram, and electrocardiograms from normal to very abnormal. The length of time after operation at which the electrocardiograms were taken ranged from two days to forty months.

None of the patients had been taking digitalis when preoperative electrocardiograms were made, but on two occasions patients were taking digitalis when tracings were made after sympathectomy.

One patient was thought to have had an acute myocardial infarction about one month before operation, and another patient was thought previously to have had a posterior myocardial infarction, but their electrocardiograms showed no evidence of such complications.

Some of the records were taken in the upright and others in the recumbent positions; in each instance, however, the postoperative electrocardiograms were taken in the same position as the respective preoperative records.

B. *Multiple Precordial Leads.*—During the last year and a half since we have been taking precordial electrocardiograms CF_2, CF_4, and CF_5 routinely on all hypertensive patients both before and after the Smithwick operation, it has become increasingly evident that they show changes as significant as those in the limb leads. The findings in these precordial leads are of diagnostic value preoperatively (see Part I of this series), and at times postoperatively they show a surprising reversal toward the normal picture. Therefore, in order to evaluate these changes a study was made of the preoperative and postoperative precordial electrocardiograms taken on forty-eight patients who have had the Smithwick lumbodorsal sympathectomy for hypertension. Patients were chosen whose preoperative tracings showed some definite abnormality in the precordial leads consistent with the diagnosis of hypertensive heart disease. In four cases the patients were on a maintenance dose of digitalis both before and after operation, but cases were omitted if they had received digitalis when the preoperative studies were done but had been taken off it before the postoperative electrocardiogram was taken, or similarly if they were given digitalis after the preoperative record was taken and kept on it postoperatively; in either instance the precordial leads would not be comparable since one set of Leads CF_2, CF_4, and CF_5 might show digitalis effect and the other might not.

The ages of the forty-eight patients ranged from 21 to 61 years with an average of 42.3 years. Electrocardiograms taken at varying intervals preoperatively were compared with similar ones taken from eight to twenty-eight days after operation, approximately two weeks afterward in half the cases. In

a small number of cases a more prolonged follow-up was available, and electrocardiograms taken up to a year after operation were compared with preoperative records.

In comparing the precordial leads taken before and after operation some difficulty was encountered because several technicians, taking tracings at intervals, often fail to place the electrode accurately at comparable locations on the chest for successive Leads CF_2, CF_4, and CF_5. Thus Lead CF_4 in one tracing may be obviously farther to the left than the same lead in another tracing. This can often be determined by observing the relative height of the R and S waves; if the R wave in Lead CF_4 of the preoperative tracing is 10 mm. high with an S wave of 9 mm. and in the postoperative record is 5 or 6 mm. higher with a proportionately smaller S wave, we suspect that the second Lead CF_4 was probably taken farther to the left since, in the accurately taken precordial leads (except in cases of myocardial infarction), the R wave is small in CF_2 and becomes progressively higher as the electrode is moved farther out on the chest, while the S wave is deep in Lead CF_2 and becomes progressively smaller in Leads CF_4 and CF_5. Other variations occur when inexperienced workers place the electrode in the fourth or sixth rather than the fifth intercostal space and when the patient has large or pendulous breasts. If these differences are overlooked, particularly in any comparative study, the results can be misleading. For example, if it is noted that the T wave in Lead CF_5 in a preoperative tracing is slightly inverted while in the similarly marked lead in the postoperative record the T wave is upright, the change might be interpreted as indicating improvement. However, if it is also observed that the R wave is of greater amplitude in the preoperative tracing than in the postoperative one, it is probable that the two leads were not taken exactly at the anterior axillary line and that the preoperative record with its higher R wave and slightly inverted T wave was therefore taken farther toward the left than was the postoperative record with its lower R wave. Hence the fact that the T wave is upright on the follow-up tracing may lose its significance since another Lead CF_5 taken correctly a few centimeters farther to the left might still show an inverted T wave.

POSTOPERATIVE CHANGES WHICH OCCURRED IN THE ELECTROCARDIOGRAM

A. *Limb Leads.*—These changes varied considerably depending upon the type and extent of the abnormality produced by the hypertension and upon the extent to which the strain on the left ventricle was relieved. Usually they were favorable, but occasionally they were unfavorable. Numerous alterations occurred in the shape of the RS-T segments, but only the significant changes will be stressed. The RS-T junction and the RS-T segment shifted in the same direction as the T waves but to a lesser degree; often the change was insignificant and difficult to measure, especially in Leads II and III. Changes in these three variables appeared to occur simultaneously although the relative change in each varied considerably in different cases. As the last portion of the RS-T segment and the first portion of the T wave in Lead I tended to become lower, flat, or even inverted during left ventricular "strain,"[7] opposite changes tended to occur after the strain was removed (Figs. 1 to 7, inclusive).

Associated with improvement in the height of the T wave in Lead I, the most frequent simultaneous alteration in Lead III was a lowering of the T wave (Figs. 1, 5, and 6). Many times an upright T wave in Lead III became inverted, as it should be normally in certain individuals (Figs. 1, 3, 4, and 7). Not uncommonly, hypertension caused a depression of the T waves in Lead III,

as well as in Lead I. Thus, if the T wave in Lead III was normally inverted, it would in some persons become more so during the "strain." In these cases, improvement consisted of elevation of the T waves in all leads (Figs. 3, 4, and 7).

Changes in Lead II were always in the same direction as those in Lead I. In the group in which improvement was associated with elevation of the T wave in Lead I and depression in Lead III, predominant changes occurred in Lead I. The T wave in Lead II, therefore, became elevated but to a lesser degree than that in Lead I, since Lead II is the algebraic sum of Leads I and III. In the group in which improvement was associated with elevation of the T waves in all leads, the T wave in Lead II became more elevated than that in Lead I for the same reason.

Improvement occurred in Lead IV, as well as in the standard leads; however, Lead IV was not included in our analyses because it was impossible to be certain that the chest electrode was at the apex in a given case, and a shift of the electrode in any direction changed the configuration of the electrocardiogram. As already noted, however, multiple precordial leads (CF_2, CF_4, and CF_5) were studied and the results will be presented later in this paper.

Concomitant with alterations in the T waves were changes in the electrical axis. Usually, the changes were in accord, that is, when the T wave improved, the electrical axis usually did likewise, and vice versa. Occasionally, however, improvement occurred in one while "unfavorable" changes occurred in the other.

Postoperative changes in the T waves, axis deviation, and the electrocardiogram as a whole are shown in Table I. T waves were referred to instead of RS-T segments because more striking changes occurred in the T waves. The T wave in Lead I was used in this analysis, as well as the remaining analyses, because the most consistent and usually the most marked changes occurred in the T waves in this lead. The T waves and electrical axis varied slightly from time to time, both before and after operation, and therefore standards (not stringent) were set up by which most of these minor changes could be eliminated from our statistics. In calculating the number of electrocardiograms which improved, minimal criteria were utilized on only five occasions, and only twice were electrocardiograms considered improved when there was considerable improvement in either the T wave or axis and only slight "unfavorable" change in the other (Fig. 3 is an example). The reason the electrocardiogram as a whole improved more often than the axis or T wave alone was that, not uncommonly, the T wave or axis improved while the other remained unchanged, according to our criteria.

These figures were based on analysis of all limb-lead postoperative electrocardiograms. If only tracings taken later than six months after operation

TABLE I. POSTOPERATIVE ELECTROCARDIOGRAPHIC CHANGES IN THE LIMB LEADS

NUMBER OF ECG'S	T WAVE*			AXIS		
	S	I	W	S	I	W
87	39 (44.8%)	41 (47.1%)	7 (8.1%)	50 (57.5%)	26 (29.8%)	11 (12.7%)

	ECG AS A WHOLE		
	S	I	W
87	26 (29.8%)	50 (57.5%)	11 (12.7%)

Referring to T waves or electrical axis: S = same or no change (i.e., less than 1 mm. elevation or depression of T, or less than 15° of change in axis); I = improvement (favorable change in T or axis beyond these limits); W = worse (unfavorable change).

Referring to ECG as a whole: S = no change in T or axis; I = improvement in T or axis with no change in the other, improvement in both, or considerable improvement in one with only slight unfavorable change in the other; W = unfavorable change using same criteria.

*T wave = T in Lead I unless otherwise specified.

were considered, statistics on the electrocardiogram as a whole would have been as follows: of fifty-six electrocardiograms, seventeen (30.3 per cent) were unchanged, thirty-five (62.6 per cent) improved, and four (7.7 per cent) were worse. This may have been the more important group since possible nonspecific effects of the operation should have disappeared by the time the records were taken.

B. *Multiple Precordial Leads.*—Changes in the QRS complexes before and after operation were not impressive. There was no change in the shape of the complexes in the comparable leads and no difference in the length of the QRS intervals. The voltage of the R and S waves varied widely, but they did not, apparently, show any constant changes related to improvement in the T waves, and the average height of the R and S waves in the individual leads before and after operation was approximately the same. In Lead CF_2 before operation the average height of the R wave was 3.4 mm. and of the S wave 20 mm.; after operation the average height of the R wave was 6.9 mm. and of the S wave 18.1 millimeters. In Lead CF_4 the average height of the preoperative R wave of the electrocardiogram was 15.7 mm. and of the S wave 9.4 mm. as compared with 15.2 mm. and 9.2 mm. postoperatively. In Lead CF_5 preoperative measurements of the R wave averaged 16.6 mm. and of the S wave 1.9 mm., while postoperatively the averages were 14.1 and 1.9 mm., respectively.*

A few of the postoperative chest leads which showed improvement in the T waves had increased voltage, and a few had decreased voltage of the QRS complexes; the voltage of the majority remained the same. Hence the changes in the QRS complexes seem to have at present little significance in evaluating postoperative improvement.

The RS-T segments also show little constant change which can be said to indicate improvement in the postoperative tracings. The RS-T segments in Lead CF_2 in preoperative records were elevated from 0.5 to 3 mm. with an average elevation of slightly over 1 mm. in forty-five, or 94 per cent, of the cases. Similarly they were elevated from 0.5 to 4 mm. postoperatively in forty-four of forty-eight, or 91 per cent, of the cases. They were never depressed in this lead either preoperatively or postoperatively. In Leads CF_4 and CF_5, both before and after operation, the RS-T segments were isoelectric in the majority of the cases. The number and percentages are as follows: preoperatively in Lead CF_4 they were isoelectric in thirty-six, or 75 per cent, of the cases and in CF_5 in thirty-three, or 69 per cent, of the cases; postoperatively they were isoelectric in CF_4 in twenty-nine, or 59 per cent, of the cases and in CF_5 in thirty-eight, or 79 per cent, of the cases. They were elevated in ten preoperative and fourteen postoperative tracings in Lead CF_4 and in three preoperative and four postoperative tracings in CF_5. They were depressed in Lead CF_4 in two cases preoperatively and in five cases postoperatively, and in Lead CF_5 in twelve cases preoperatively and in six cases postoperatively. A depression of 0.5 mm. or more in Leads CF_4 and CF_5 was usually (seventeen out of twenty-three times) associated in this series with diphasic or inverted T waves. The converse was not true, however, since inverted T waves occurred frequently with isoelectric RS-T segments. Apparently, too, the RS-T segments became isoelectric when the T waves became upright. Thus, changes in the RS-T segments apart from T-wave changes did not seem important as an indication of postoperative improvement.

As at first observed during routine readings in the Cardiac Laboratory, the T waves which are low, diphasic, or inverted in the precordial leads taken

*These results are about the same as those obtained when the R and S waves were measured in one hundred precordial electrocardiograms taken preoperatively on hypertensive patients.

TABLE II. POSTOPERATIVE ELECTROCARDIOGRAPHIC CHANGES IN THE T WAVES OF THE PRECORDIAL LEADS

NUMBER OF ECG'S	S	I					W
48	25 (52.1%)	19 (39.6%)					4 (8.3%)
		A	*B*	*C*	*D*	*E*	
		5 (10.4%)	2 (4.2%)	2 (4.2%)	4 (8.3%)	6 (12.5%)	

S = no change in T waves.

W = unfavorable change.

I = Definite improvement in the precordial electrocardiogram. *A*, marked improvement in Leads CF_4 and CF_5 with change of one or both of the T waves from inverted to upright; *B*, change from inverted to upright T waves in Lead CF_5; *C*, less deep inversion of T waves in Leads CF_4 and CF_5; *D*, increase in voltage in T waves in Leads CF_4 and CF_5; *E*, increase in voltage of T waves in Lead CF_5.

preoperatively frequently show an interesting and rather striking return toward the normal in postoperative records; we find that the changes shown are highly significant (Table II). In sixteen cases there was no change at all in the electrocardiograms taken before and after operation. To this group we added nine cases whose electrocardiograms showed such slight improvement that their significance was debatable; twenty-five of forty-eight, or 52.1 per cent, of the precordial electrocardiograms showed no noteworthy differences before and after operation.

In four, or 8.3 per cent, of the forty-eight cases the postoperative tracings became more abnormal; in one case the T wave in Lead CF_5 became 0.5 mm. lower; in two cases an isoelectric T wave in Lead CF_5 became slightly inverted; and in one case low, upright T waves in Leads CF_4 and CF_5 became deeply inverted.

In nineteen cases, or 39.6 per cent, there was clear-cut improvement in the postoperative electrocardiogram, and we subdivided this group according to the leads involved and the degree of change (Table II). In eight cases there was definite improvement of the T wave in Lead CF_5 as follows: in six cases there was an increase in voltage of from 0.5 to 1.5 mm.; in two cases there was marked improvement, inverted T waves becoming upright and of normal voltage. In eleven cases there was a definite improvement in the T waves in both Leads CF_4 and CF_5 as follows: in two cases the T waves were less deeply inverted after operation, in four cases there was an increase in the amplitude of the T waves of from 1 to 5 mm., and in five cases there was a marked change toward the normal with either one or both of the T waves, which had previously been inverted, becoming upright. One case not included in the forty-eight showed an increase in voltage of 3 mm. in the T wave in Lead CF_4 and 2 mm. in the T wave in Lead CF_5 postoperatively; the preoperative record was entirely within normal limits. Another case, also not included in the present statistical study, showed return of inverted T waves postoperatively; this electrocardiogram could not be evaluated because digitalis had been discontinued for two weeks so that some or even all of the improvement might possibly have been due to the clearing of the digitalis effect.

CORRELATIONS

In Table III postoperative limb-lead electrocardiographic changes were correlated with preoperative eye-ground findings. Criteria for grading the eye grounds were as follows: Normal, no abnormal findings in the retina; Grade 1, minimal caliber changes in the retinal arterioles; Grade 2, caliber variations

TABLE III. CORRELATION OF POSTOPERATIVE LIMB-LEAD ELECTROCARDIOGRAPHIC CHANGES WITH PREOPERATIVE EYE-GROUND CLASSIFICATION

EYE GROUNDS	NUMBER OF ECG'S	T CHANGES S	T CHANGES I	T CHANGES W	AXIS CHANGES S	AXIS CHANGES I	AXIS CHANGES W
Normal	1	0 (0%)	1 (100%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)
Grade 1	30	18 (60.0%)	11 (36.7%)	1 (3.3%)	19 (63.3%)	6 (20.0%)	5 (16.7%)
Grade 2	24	8 (33.3%)	13 (54.2%)	3 (12.5%)	18 (75.0%)	3 (12.5%)	3 (12.5%)
Grade 3	23	11 (47.8%)	11 (47.8%)	1 (4.4%)	10 (43.5%)	11 (47.8%)	2 (8.7%)
Grade 4	9	2 (22.2%)	5 (55.6%)	2 (22.2%)	2 (22.2%)	6 (66.7%)	1 (11.1%)

EYE GROUNDS	NUMBER OF ECG'S	ECG AS A WHOLE S	ECG AS A WHOLE I	ECG AS A WHOLE W
Normal	1	0 (0%)	1 (100%)	0 (0%)
Grade 1	30	13 (43.3%)	12 (40%)	5 (16.7%)
Grade 2	24	7 (29.2%)	13 (54.2%)	4 (16.6%)
Grade 3	23	6 (26.1%)	16 (69.6%)	1 (4.3%)
Grade 4	9	0 (0%)	8 (88.9%)	1 (11.1%)

with arteriovenous nicking; Grade 3, hemorrhages and exudates; Grade 4, changes as in Grade 2 plus papilledema.[7]

This table is of interest in that chances for improvement in the electrocardiogram increased as the eye grounds became worse.

TABLE IV. CORRELATION OF POSTOPERATIVE LIMB-LEAD ELECTROCARDIOGRAPHIC CHANGES WITH RENAL BIOPSIES

RENAL GRADE	NUMBER OF ECG'S	S	I	W
0	3	1 (33.3%)	2 (66.6%)	0 (0%)
1	11	5 (45.4%)	5 (45.4%)	1 (9.2%)
2	18	7 (38.9%)	8 (44.4%)	3 (16.7%)
3	28	6 (21.4%)	20 (71.4%)	2 (7.2%)
4	9	2 (22.2%)	3 (33.3%)	4 (44.5%)

In Table IV postoperative limb-lead electrocardiographic alterations were correlated with pathologic changes found in biopsy material taken from the kidneys at the time of operation. The biopsies were classified in five groups as follows: Grade 0, no abnormal findings seen; Grade 1, slight amount of vascular change (predominantly arteriolar intimal hyalinization and arterial endothelial hyperplasia); Grade 2, slightly more vascular change than in Grade 1 with an occasional hyalinized glomerulus; Grade 3, severe vascular disease in every vessel with predominant medial arteriolar hypertrophy and many hyalinized glomeruli; Grade 4, involvement of every vessel, scarring of many glomeruli, and atrophy of surrounding tubules.[8]

There appeared to be no definite correlation between postoperative electrocardiographic changes and disease in the kidneys. Only three electrocardiograms were taken on patients with normal kidneys, two of whom improved and one remained unchanged. In the group with Grade 3 kidneys, the incidence of improvement was distinctly greater and that of unfavorable change was distinctly less than in other groups. The incidence was reversed in the group with Grade 4 kidneys; however, these figures were not so statistically significant since only nine electrocardiograms were obtained in this group.

TABLE V. CORRELATION OF POSTOPERATIVE LIMB-LEAD ELECTROCARDIOGRAPHIC CHANGES WITH PREOPERATIVE HEART SIZE

HEART SIZE	NUMBER OF ECG'S	S	I	W
Normal	46	18 (39.1%)	23 (50%)	5 (10.9%)
Enlarged	38	8 (21.1%)	24 (63.2%)	6 (15.7%)

Correlations with preoperative heart size were made in Table V. The heart size in each instance was based on the roentgenologist's opinion of the teleroentgenogram. Variations in the heart size affected slightly the chances for improvement or unfavorable change in the limb-lead electrocardiogram.

Postoperative limb-lead electrocardiographic changes were correlated with the known duration of hypertension in Table VI. The number of electrocardiograms taken in the three five-year periods, from eleven to twenty-five years, was too few to be of statistical significance, but the definite lack of correlation was evident here as it was in the two five-year periods from zero to ten years.

TABLE VI. CORRELATION OF POSTOPERATIVE LIMB-LEAD ELECTROCARDIOGRAPHIC CHANGES WITH THE KNOWN DURATION OF HYPERTENSION

DURATION (YRS.)	NUMBER OF ECG'S	S	I	W
0 to 5	52	15 (28.9%)	31 (58.8%)	6 (12.3%)
6 to 10	24	7 (29.2%)	14 (58.4%)	3 (12.4%)
11 to 15	6	3 (50%)	1 (16.7%)	2 (33.3%)
16 to 20	2	1 (50%)	1 (50%)	0 (0%)
21 to 25	1	1 (100%)	0 (0%)	0 (0%)

Table VII shows that the tendency for limb-lead electrocardiograms to improve or become worse was approximately the same in the patients with dyspnea as in those without it. Two of the four records which were taken on patients who complained of chest pain improved while the other two remained unchanged, but the number of tracings was too few to draw any definite conclusions.

TABLE VII. CORRELATION OF POSTOPERATIVE LIMB-LEAD ELECTROCARDIOGRAPHIC CHANGES WITH PREOPERATIVE SYMPTOMS

SYMPTOMS	NUMBER OF ECG'S	S	I	W
None	53	19 (37.7%)	28 (52.8%)	6 (9.5%)
Dyspnea	29	6 (20.7%)	18 (62.8%)	5 (16.5%)
Pain	4	2 (50.0%)	2 (50.0%)	0 (0.0%)

That the patient's age did not affect the incidence of change in the limb-lead electrocardiogram one way or the other is shown in Table VIII.

TABLE VIII. CORRELATION OF POSTOPERATIVE LIMB-LEAD ELECTROCARDIOGRAMS WITH THE PATIENT'S AGE

AGE (YRS.)	NUMBER OF ECG'S	S	I	W
10 to 20	1	0 (0.0%)	1 (100.0%)	0 (0.0%)
21 to 30	8	3 (37.5%)	4 (50.0%)	1 (12.5%)
31 to 40	30	7 (23.3%)	19 (63.3%)	4 (13.3%)
41 to 50	41	15 (36.6%)	21 (51.2%)	5 (12.2%)
51 to 60	6	2 (33.3%)	3 (50.0%)	1 (16.7%)

Table IX reveals that the incidence of improvement in the limb-lead electrocardiogram increased and that of unfavorable change decreased as the preoperative diastolic blood pressure became higher.

TABLE IX. CORRELATION OF POSTOPERATIVE LIMB-LEAD ELECTROCARDIOGRAPHIC CHANGES WITH DIASTOLIC BLOOD PRESSURE ON ADMISSION

B.P.	NUMBER OF ECG'S	S	I	W
100 or below	3	1 (33.3%)	1 (33.3%)	1 (33.3%)
101 to 110	17	4 (23.5%)	9 (53.0%)	4 (23.5%)
111 to 120	16	10 (62.5%)	4 (25.0%)	2 (12.5%)
121 to 130	11	4 (36.4%)	6 (54.5%)	1 (9.1%)
131 to 140	19	5 (26.3%)	13 (68.4%)	1 (5.2%)
Over 140	19	2 (10.5%)	15 (79.0%)	2 (10.5%)

Table X reveals a tendency to positive correlation between long-term improvement in the limb-lead electrocardiogram and long-term improvement in the diastolic blood pressure following sympathectomy.

TABLE X. CORRELATION BETWEEN CHANGES IN THE LIMB-LEAD ELECTROCARDIOGRAM AND THE DIASTOLIC BLOOD PRESSURE LATER THAN SIX MONTHS AFTER OPERATION

ECG	NUMBER OF ECG'S	DIASTOLIC BLOOD PRESSURE		
		S	I	W
Unchanged	17	3 (17.6%)	13 (76.5%)	1 (5.9%)
Improved	40	8 (20.0%)	29 (72.5%)	3 (7.5%)
Worse	4	1 (25.0%)	2 (50.0%)	1 (25.0%)

S = No change (using same criteria).
I= Improved (a decrease of 10 mm. Hg. when diastolic pressure is 110 or below, 15 mm. at 111 to 130,and 20 mm. over 130).
W = Worse (an increase beyond these limits).

Table XI presents the correlation between changes in the T waves of the precordial electrocardiogram and changes in the diastolic blood pressure following operation. In general there was agreement, but there were four exceptions in which the electrocardiogram became worse even though the diastolic pressure was improved postoperatively.

TABLE XI. CORRELATION BETWEEN CHANGES IN THE T WAVES OF THE PRECORDIAL ELECTROCARDIOGRAM AND THE DIASTOLIC BLOOD PRESSURE

ECG	NUMBER OF ECG'S	DIASTOLIC BLOOD PRESSURE		
		S	I	W
Unchanged	25	7 (28%)	17 (68%)	1 (4%)
Improved	19	4 (21%)	15 (79%)	0
Worse	4	0	4 (100%)	0
Total	48	11 (23%)	36 (75%)	1 (2%)

S = No change (using same criteria).
I = Improved (a decrease of 10 mm. Hg when diastolic pressure is 110 or below, 15 mm. at 111 to 130, and 20 mm. over 130).
W = Worse (an increase beyond these limits).

There was some relationship between limb-lead electrocardiographic changes and the length of time after operation at which the records were taken (Table XII). The incidence of improvement was distinctly greater and that of unfavorable change distinctly less during the second six-month period.

TABLE XII. CORRELATION OF POSTOPERATIVE LIMB-LEAD ELECTROCARDIOGRAMS WITH LENGTH OF TIME AFTER OPERATION

POSTOPERATIVE TIME	NUMBER OF ECG'S	ECG CHANGES		
		S	I	W
1 to 6 months	31	10 (32.2%)	14 (45.2%)	7 (22.5%)
7 to 12 months	23	5 (21.7%)	18 (78.3%)	0 (0%)
1 to 2 years	18	9 (50%)	8 (44.4%)	1 (5.6%)
2 to 3 years	13	3 (23.1%)	7 (53.8%)	3 (23.1%)
3 to 4 years	2	0 (0%)	2 (100%)	0 (0%)

The more abnormal the T wave in Lead I before operation, the greater the chances for its improvement after sympathectomy, as can be seen in Table XIII. When the T wave was at the borderline of normal (1 mm. or over) 35.7 per cent improved and 14.3 per cent became worse, but when it was inverted

TABLE XIII. CORRELATION OF THE HEIGHT OF THE T WAVE IN LEAD I BEFORE AND AFTER OPERATION

HEIGHT OF T_1	NUMBER OF ECG'S	S	I	W
1 mm. or over	42	21 (50.0%)	15 (35.7%)	6 (14.3%)
Below 1 mm. but not inverted	10	3 (30.0%)	7 (70.0%)	0 (0.0%)
Diphasic to -2 mm.	21	8 (38.1%)	11 (52.4%)	2 (9.5%)
Below -2 mm.	14	3 (21.4%)	11 (78.6%)	0 (0.0%)

more than 2 mm., 78.6 per cent improved, while none became worse (the other 21.4 per cent remained unchanged).

Other preoperative electrocardiographic findings which may have influenced changes after sympathectomy were Q waves in any of the standard leads and T-wave changes in Leads II and III. One of the two patients operated upon who had abnormal Q waves in Lead I died during induction of anesthesia. In this patient the Q wave in Lead I was 2 mm. and the greatest amplitude of the RS-T deflections was 10 millimeters. The patient was thought to have died of myocardial infarction but permission for necropsy was not obtained. No follow-up electrocardiogram has been obtained on the other patient. No untoward reactions occurred in any of the fourteen patients with large Q waves in Lead III. Postoperative electrocardiograms were obtained on four of these. One Q wave of 4 mm. remained unchanged thirteen months after operation, and there were no other changes in the electrocardiogram. Another changed from a QS wave of 10 mm. to a Q wave of 7 millimeters. The axis improved but the T waves remained unchanged. In another the Q wave changed from 3.5 to 1.5 mm. without any other change in the record. The fourth electrocardiogram remained unchanged. There were no abnormal Q waves in Lead II in any electrocardiogram.

No deleterious results occurred in any of the seven patients with inverted T waves in all three limb leads or in the fourteen with inverted T waves in Leads II and III. There were no abnormal Q waves in either group.

Of the five patients with inverted T waves in all three limb leads who had follow-up tracings, the electrocardiograms improved in two (all T waves became less inverted), remained unchanged in two, and became worse in one. Of the four patients with inverted T waves in Leads II and III who had follow-up tracings, the electrocardiograms improved in three and remained unchanged in the other.

Four patients were thought to have died cardiac deaths during the period of study. One died during induction of anesthesia before operation. This was the patient already referred to whose electrocardiogram showed a Q wave of 2 mm. in Lead I with a maximal QRS deflection of 10 mm. but no other abnormality. One patient died in uremia after myocardial infarction ten days following the first-stage operation. His electrocardiogram showed a slight depression of the RS-T segment with an inverted T wave in Lead I and a diphasic T wave in Lead II. Another died three weeks postoperatively from extensive coronary disease, but no fresh infarction could be found at necropsy. The RS-T segment was slightly depressed and the T wave diphasic in Lead I. Another died from myocardial infarction with normal blood pressure two years after sympathectomy.

DISCUSSION OF INDIVIDUAL CASES

A few of the cases in which the electrocardiogram* improved (Figs. 1 to 7 and 8 to 12, inclusive) are as follows:

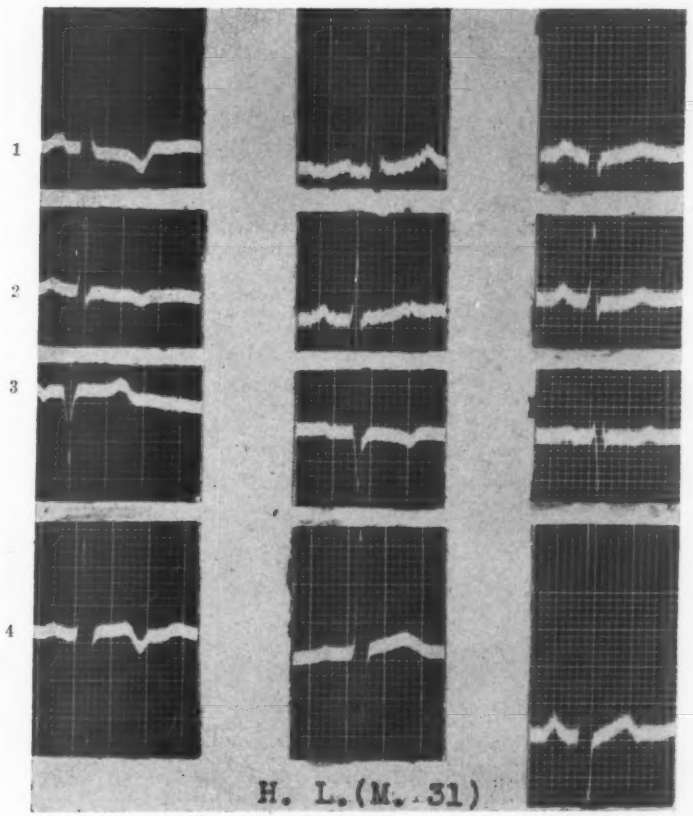
CASE 1.—H. L., a 31-year-old man, was admitted to the Massachusetts General Hospital on Sept. 9, 1942, because of severe hypertension discovered on a routine insurance examination four months previously. He had been having mild morning occipital headaches for two months and recently dyspnea on exertion.

On physical examination his blood pressure was found to be 165/136. Auscultation of his heart revealed early diastolic and presystolic gallop sounds, which were substantiated by sound tracings. His eye grounds were classified as Grade 1 (variation in caliber of the vessels).

*The first tracing in each instance was taken before sympathectomy. The other tracings were taken at variable intervals after operation.

Teleroentgenograms revealed some pulmonary congestion and rounding of the cardiac apex. An electrocardiogram (Fig. 1) revealed depression of the RS-T segment in Lead I with inversion of the T waves in Leads I, II, and IVF, a large QS (9 mm.) and elevation of the RS-T segment and T wave in Lead III, and slight left axis deviation.

He was given two ampules of Digifolin preoperatively. The first stage of the bilateral sympathectomy was carried out on Oct. 1, 1942, and the second stage of his operation was performed on Oct. 13, 1942. Renal biopsies showed Grade 3 chronic vascular nephritis. The gallop rhythm disappeared, his blood pressure dropped to 120/70 to 80/50, and on Nov. 3, 1942, his electrocardiogram was within normal limits. The RS-T segments had become elevated in Lead I and depressed in Lead III. The T waves had become upright in Leads I, II, and IVF and inverted in Lead III. Predominant changes occurred in Lead I, therefore, and the T wave in Lead II was elevated. Six months later he was feeling well and working hard. His blood pressure was 110/60, and his electrocardiogram was still within the range of normal. The QS in Lead III had changed to RSR'. At the end of 1944, two years after his operation, he was in good health with normal blood pressure.



A. *B.* *C.*

Fig. 1.—H. L., a man, aged 31 years. *A*, Electrocardiogram taken Oct. 9, 1942; blood pressure, 165/136. *B*, Taken Nov. 3, 1942; blood pressure, 120/70 to 80/50. *C*, Taken April 15, 1943; blood pressure, 110/60. Sympathectomy Oct. 13, 1942.

CASE 2.—L. K., a 29-year-old woman, was admitted to the Massachusetts General Hospital on Sept. 25, 1940, with a history of having had high blood pressure (up to 270/170) and headaches for two years.

On physical examination her blood pressure was found to be 240/150. Her eye grounds were classified as Grade 4 (papilledema). Her heart was not enlarged, and numerous tests were found to be within normal limits. Her electrocardiogram (Fig. 2) showed a depression of the RS-T segment and inversion of the T wave in Lead I.

The second stage of her sympathectomy was completed on Oct. 16, 1940. At the time of her postoperative check-up on Jan. 13, 1943 (twenty-eight months after operation), her blood pressure was 140/90 and her eye grounds and electrocardiogram were normal. The RS-T segments in Leads I and II and the T waves in Leads I, II, and III had become more

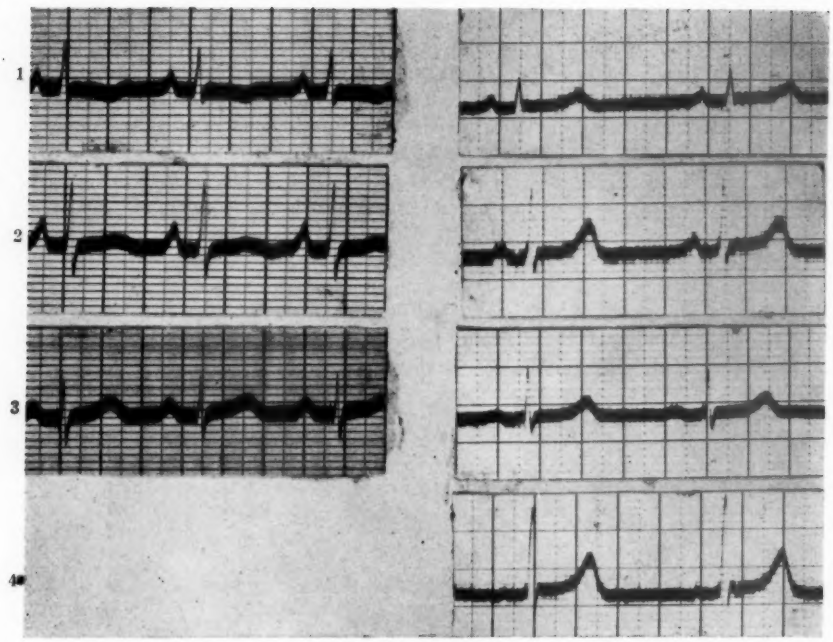


Fig. 2.—L. K., a woman, aged 29 years. *A*, Electrocardiogram taken Sept. 28, 1940; blood pressure, 250/140. *B*, Taken Jan. 13, 1943; blood pressure, 140/90. Sympathectomy Oct. 16, 1940.

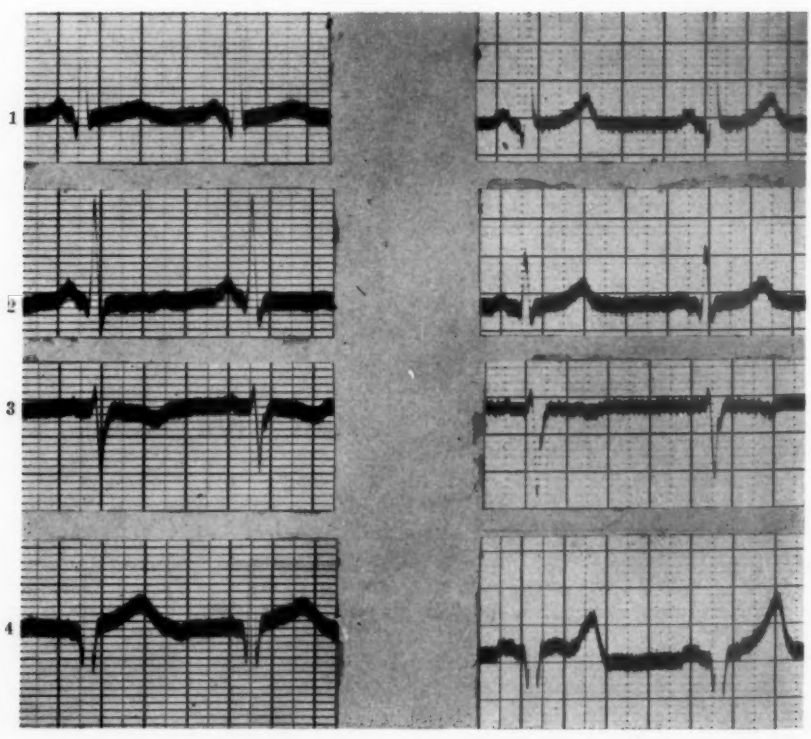


Fig. 3.—J. S., a man, aged 46 years. *A*, Electrocardiogram taken Dec. 6, 1940; blood pressure, 210/140 (lying), 180/135 (standing). *B*, Taken March 25, 1943; blood pressure, 195/145 (lying), 139/119 (standing). Sympathectomy Dec. 21, 1940.

elevated; predominant changes occurred in Lead II. There was slight improvement in the electrical axis. Ten months later, at the end of 1943, over three years after operation, the blood pressure was still normal (120/76).

CASE 3.—J. S., a 46-year-old man, who was known to have had a blood pressure of 170/110 six years previously, was admitted to the Massachusetts General Hospital on Nov. 10, 1940, with a history of having had dyspnea on exertion and dizziness for three years, and severe headaches, weakness, and blurring of vision for three weeks.

Physical examination revealed a blood pressure of 210/140, lying, and 180/135, standing. Exudates and hemorrhages were found in the eye grounds (Grade 3).

His urine contained much albumin (3 plus), many coarsely and finely granular casts, and occasional red blood cells. An intravenous phenolsulfonphthalein test showed an excretion of 5 per cent of the dye in fifteen minutes and 40 per cent in two hours. The electrocardiogram (Fig. 3) revealed slight left axis deviation, slight depression of RS-T segments, and inversion of the T waves in Leads II and III. A small Q wave (2 mm.) was present in Lead I and a slightly larger one (3.5 mm.) was present in Lead IV.

A bilateral sympathectomy was performed in December, 1940, when renal biopsies revealed Grade 3 vascular nephritis and chronic pyelonephritis.

Fourteen months after operation his blood pressure was found to be 106/60, but no electrocardiograms were taken. On March 25, 1943 (twenty-seven months after operation), his blood pressure was 195/145, lying, and 139/119, standing, and his eye grounds failed to show exudates or hemorrhages. His phenolsulfonphthalein test showed a 23 per cent excretion of the dye in fifteen minutes and 55 per cent in two hours. His electrocardiogram was within normal limits—the RS-T segments and T waves in the three standard leads had become more elevated; maximal changes occurred in Lead II. There were no changes in the Q waves. He was well and doing full-time strenuous work. Nine months later, three years after operation, his blood pressure was satisfactory, at 151/106.

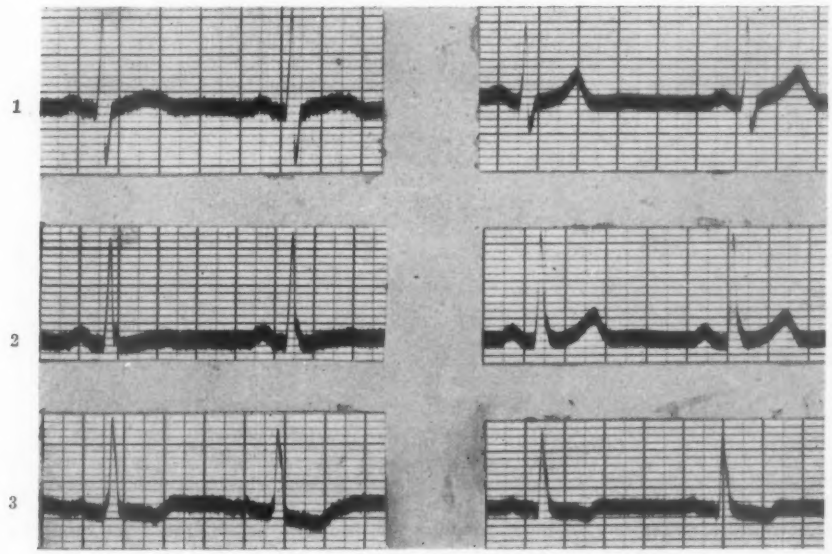


Fig. 4.—W. T., a man, aged 35 years. *A*, Electrocardiogram taken May 6, 1942; blood pressure, 200/145. *B*, Taken Nov. 2, 1942; blood pressure, 130/90. On May 3, 1943, the blood pressure was 122/76. Sympathectomy May 26, 1942.

CASE 4.—W. T., a 35-year-old man, was admitted to the Massachusetts General Hospital on May 6, 1942, with a history of having had dizzy spells for two to three years, incapacitating frontal headaches for several months, and weakness for four months. He had also had palpitation and slight dyspnea on exertion.

Physical examination revealed a blood pressure of 200/145 and Grade 2 eye grounds (a-v nicking). His heart size was at the upper limits of normal by teleroentgenogram. An electrocardiogram (Fig. 4) revealed a depression of the RS-T segment in Leads II and III with notching of the T wave in Lead II and inversion in Lead III. There was a prominent S wave in Lead I.

Six months after operation, his blood pressure was 132/76, but unfortunately electrocardiograms were not taken at that time. On May 3, 1943 (one year after operation), his blood pressure was 130/90, he was doing strenuous work, and he felt well. His electrocardiogram was now within normal limits. The RS-T segments and T waves had become more elevated in the three leads; maximal changes again occurred in Lead II.

CASE 5.—M. B., a 43-year-old woman, was admitted to the Massachusetts General Hospital on Nov. 15, 1939, because of hypertension which had been diagnosed two years previously. She had been having headaches for three to four years and blurring of vision for two years.

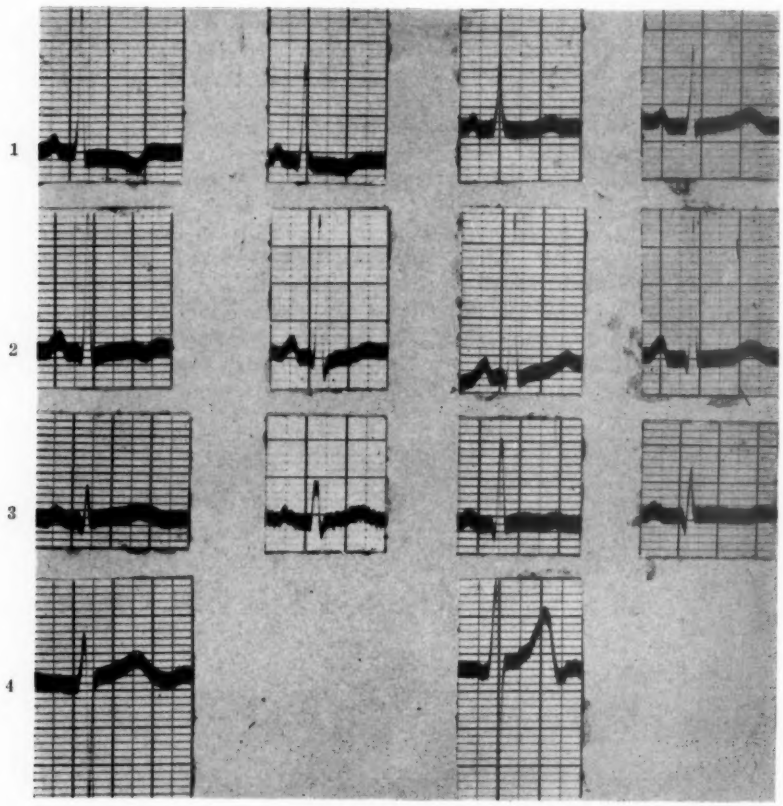


Fig. 5.—M. B., a woman, aged 43 years. *A*, Electrocardiogram taken Oct. 15, 1939; blood pressure, 260/110 (lying), 190/110 (standing). *B*, Taken Dec. 26, 1939. *C*, Taken Feb. 9, 1940. *D*, Taken Nov. 25, 1941; blood pressure, 180/110 (lying), 140/100 (standing). Sympathectomy Dec. 21, 1939.

On physical examination her blood pressure was found to be 200/110, lying, and 190/110, standing. Her eye grounds were classified as Grade 3. Teleroentgenograms revealed enlargement of the left ventricle. An electrocardiogram (Fig. 5) showed depression of the RS-T segments in Leads I and II and slight elevation in Lead III. T waves in Leads I and II were inverted.

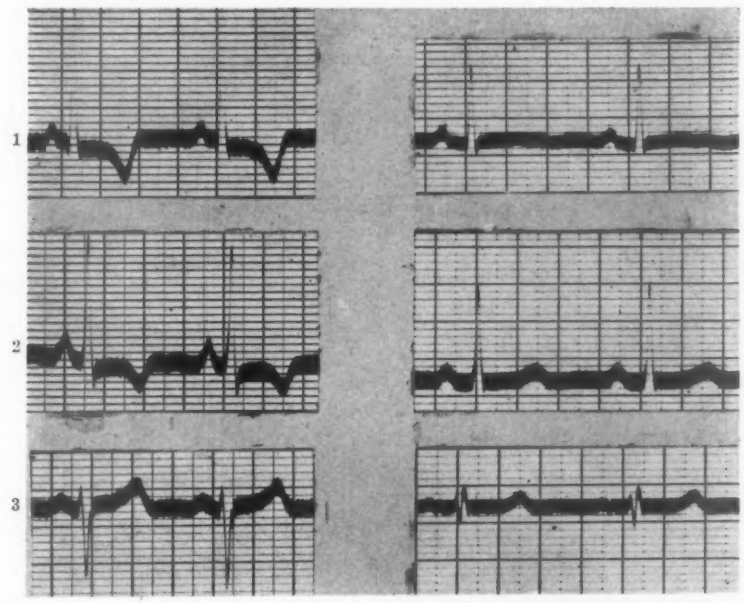
Sympathectomy was performed on Dec. 21, 1939. The blood pressure measured 138/92 three weeks later and 177/110 two years after operation. Electrocardiograms taken five days, seven weeks, and twenty-six months, respectively, after operation showed a gradual return to normal. The RS-T segments in Leads I and II became elevated, and those in Lead III depressed. The T wave in Lead III was now inverted.

These records are of interest in that the relative postural hypotension was apparently sufficient to relieve the heart of considerable strain over a period of more than two years, as in Case 3. During this time the patient was feeling well without symptoms. Her usual pressure at home was probably well below our figures.[9]

CASE 6.—M. O., a 39-year-old woman, was admitted to the Massachusetts General Hospital on Nov. 11, 1941, with a history of having had headaches, dizzy spells, moderate dyspnea, palpitation, and occasionally substernal pain radiating down the left arm on climbing a flight of stairs, for about five months.

On physical examination her heart was slightly enlarged, her blood pressure was 180/110, and her eye grounds showed a-v nicking. An electrocardiogram revealed depression of the RS-T segments, inversion of the T waves in Leads I and II, and elevation of the T waves in Lead III (Fig. 6).

A sympathectomy was performed in March, 1942. Over thirteen months later her blood pressure was 150/100, and her electrocardiogram was almost normal. There were striking changes in the RS-T segments and axis. RS-T segments and T waves had become elevated in Leads I and II and depressed in Lead III.



A. *B.*

Fig. 6.—M. O., a woman, aged 39 years. *A*, Electrocardiogram taken Dec. 4, 1941; blood pressure, 180/110. *B*, Taken April 26, 1943; blood pressure, 150/100. Sympathectomy March 7, 1942.

CASE 7.—A. R., an 18-year-old man, was admitted to the Massachusetts General Hospital on Jan. 15, 1942, with a history of having had headaches for six months and palpitation, blurring of vision, mental confusion, and right facial paralysis for three days.

On physical examination his blood pressure was found to be 190/140. There was slight pulsus alternans and his eye grounds showed exudates and hemorrhages. By teleroentgenogram his heart was moderately enlarged. His electrocardiogram showed depression of the RS-T segments and inversion of the T waves in Leads II and III (Fig. 7).

A right lumbar sympathectomy and excision of a renal tumor (pheochromocytoma) were performed on Feb. 10, 1942.

On Nov. 23, 1942 (nine months after operation), he was feeling well, and his blood pressure was 116/76. His electrocardiogram was now within normal limits. The RS-T segments and T waves had become more elevated, but the T wave in Lead III was still inverted.

CASE 8.—L. H. DeW., a 35-year-old male college professor, entered the Massachusetts General Hospital in April, 1940, because of tonsillitis. His blood pressure was then normal (124/80). He re-entered the hospital on May 29, 1944, because of headaches, dyspnea, and hypertension which had been discovered in 1942 at the time of an insurance examination; he was rejected on the discovery of readings of 190/130.

Physical examination at the time of his second hospital admission showed no abnormalities except for the hypertension of 190/130. Ophthalmoscopic examination showed Grade 2

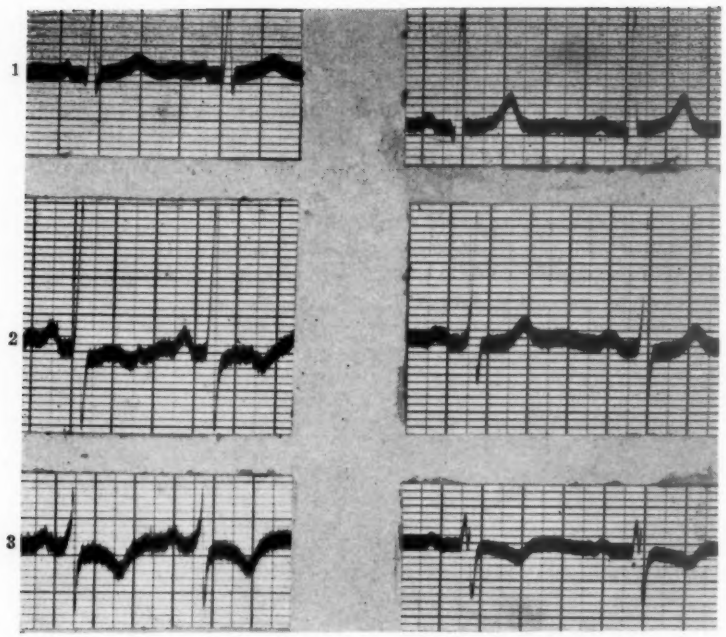


Fig. 7.—A. R., a man, aged 18 years. *A*, Electrocardiogram taken Jan. 20, 1942; blood pressure, 190/140. *B*, Taken Nov. 23, 1942; blood pressure, 110/76. Right lumbar sympathectomy and excision of pheochromocytoma, Feb. 10, 1942.

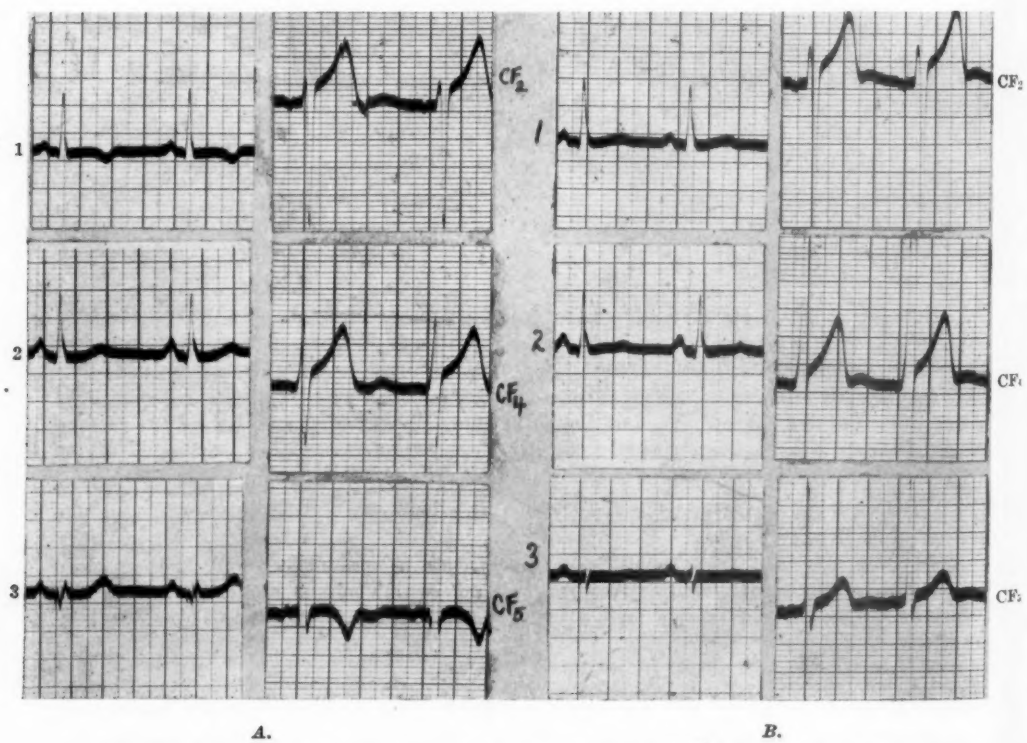
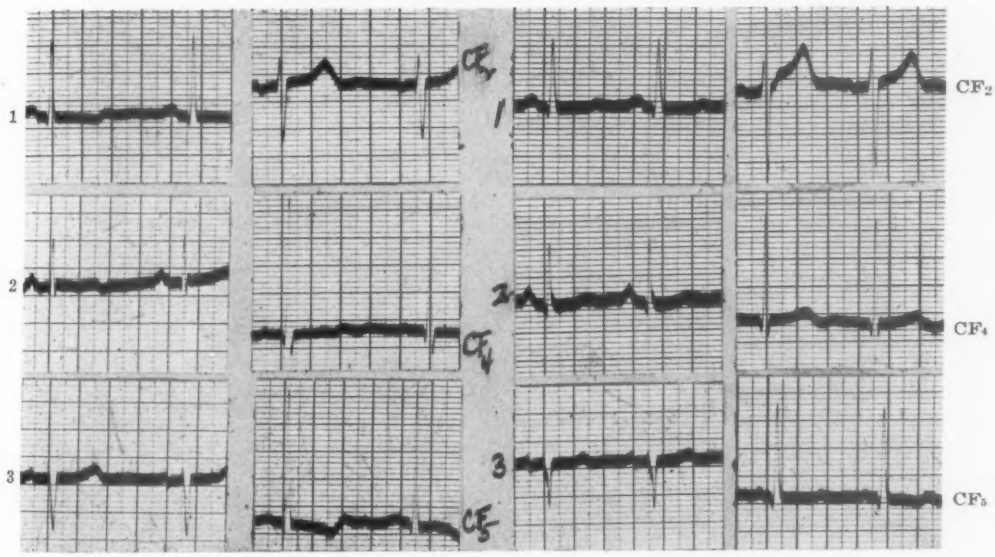


Fig. 8.—L. H. DeW., a man, aged 39 years. *A*, Electrocardiogram taken May 30, 1944; blood pressure 190/130. *B*, Taken June 21, 1944; blood pressure, 145/105. Sympathectomy May 31 and June 9, 1944.

hypertensive and Grade 3 arteriosclerotic fundi. The electrocardiogram (Fig. 8, *A*) showed normal rhythm (rate 70), normal axis, and late inversion of the T waves in Leads I and CF_5, characteristic of "left ventricular strain." The blood was normal. The urine showed 0 to a very slight trace of albumin, with specific gravity of 1.018 to 1.024, and a few blood cells in the sediment. The renal function (phenolsulfonphthalein) test gave a reading of 62 per cent in one hour. Blood nonprotein nitrogen was 22 to 35 mg. per cent.

Bilateral lumbodorsal sympathectomy was carried out May 31 and June 9, 1944, without complications. He was discharged June 23 with a blood pressure of 130/95. His electrocardiogram (Fig. 8, *B*) taken on June 21, when his pressure was 145/105, showed normal rhythm (rate 85), with a low but upright T wave in Lead I and upright T waves in all three precordial leads—a marked improvement.

CASE 9.—M. A. W., a 50-year-old female clerk, entered the Massachusetts General Hospital, Sept. 18, 1944, because of hypertension of nine years' known duration, and right hemiplegia in the fall of 1943, which had left little residuum. There had been some dyspnea on effort.



A. *B.*

Fig. 9.—M. A. W., a woman, aged 50 years. *A*, Electrocardiogram taken Sept. 15, 1944; blood pressure, 240/130. *B*, Taken Oct. 9, 1944; blood pressure, 170/110. Sympathectomy Sept. 19 and 29, 1944.

Physical examination on admission showed nothing amiss except for slight cardiac enlargement and a blood pressure of 240/130. Ophthalmoscopic examination showed Grade 2 hypertensive and Grade 3 arteriosclerotic fundi. X-ray examination showed a heart of full size, normal aorta, and clear lungs. The electrocardiogram (Fig. 9, *A*) on Sept. 15, 1944, showed normal rhythm (rate 70), slight left axis deviation, with almost flat, diphasic T waves in Lead I, very low T waves in Leads II and CF_4, high R waves in Leads CF_4 and CF_5, and inverted T waves in Lead CF_5. The blood and urine were normal. The renal function (phenolsulfonphthalein) test showed 55 per cent in one hour. Blood pressure reactions to posture, cold, and sedation were characteristic and favorable.

Bilateral lumbodorsal sympathectomy was done on September 19 and 29 without complications. She was discharged from the hospital October 20 with a blood pressure reading of 155/110. The electrocardiogram (Fig. 9, *B*) on October 9, when the pressure registered 170/110, showed normal rhythm (rate 85), very slight left axis deviation, and low but upright T waves in Leads I, CF_4, and CF_5—a slight but definite improvement.

CASE 10.—B. K., a 27-year-old housewife, entered the Massachusetts General Hospital Dec. 9, 1943, for hypertension which had been discovered in January, 1943. There had been no symptoms.

Physical examination on entrance to the hospital showed no abnormalities except for the hypertension (220/160). Ophthalmoscopic examination revealed Grade 2 hypertensive fundi,

X-ray examination showed apparently normal heart, lungs, and pyelogram. The electrocardiogram (Fig. 10, *A*), taken December 13, showed normal rhythm (rate 85), with normal limb leads but inverted T waves in Lead CF_4 and diphasic T waves in Lead CF_5. The blood was normal and showed 31 mg. per cent of nonprotein nitrogen. The urine showed slight albuminuria, specific gravity up to 1.018, and a moderate number of white and red blood cells without casts in the sediment. The renal function (phenolsulfonphthalein) test registered 60 per cent in one hour.

Bilateral lumbodorsal sympathectomy was carried out on December 18 and 29 without complications. She was discharged January 18, 1944, with a blood pressure reading of 160/118. An electrocardiogram (Fig. 10, *B*) taken January 14, when the blood pressure measured 180/110, showed normal rhythm (rate 80) and normal T waves in all six leads, a distinct improvement in the precordial leads over the preoperative record.

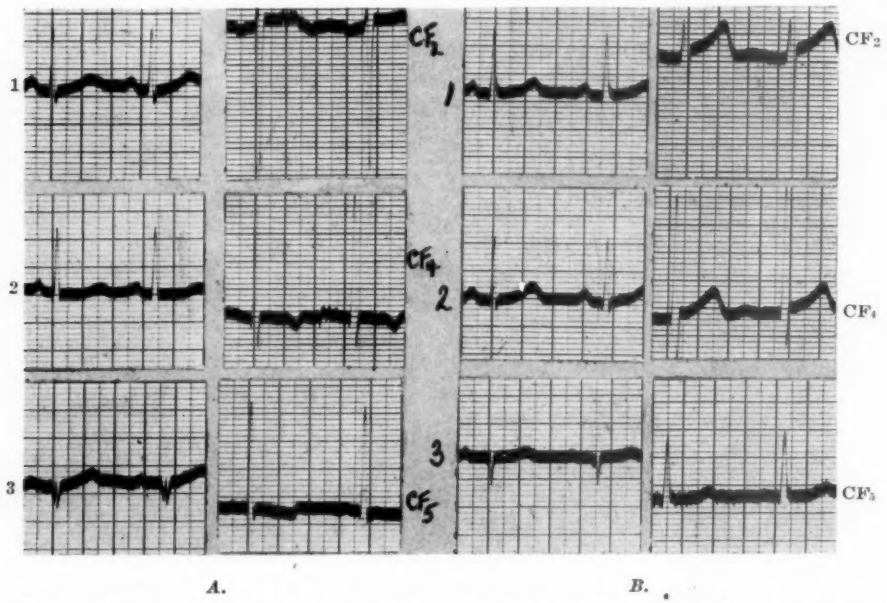


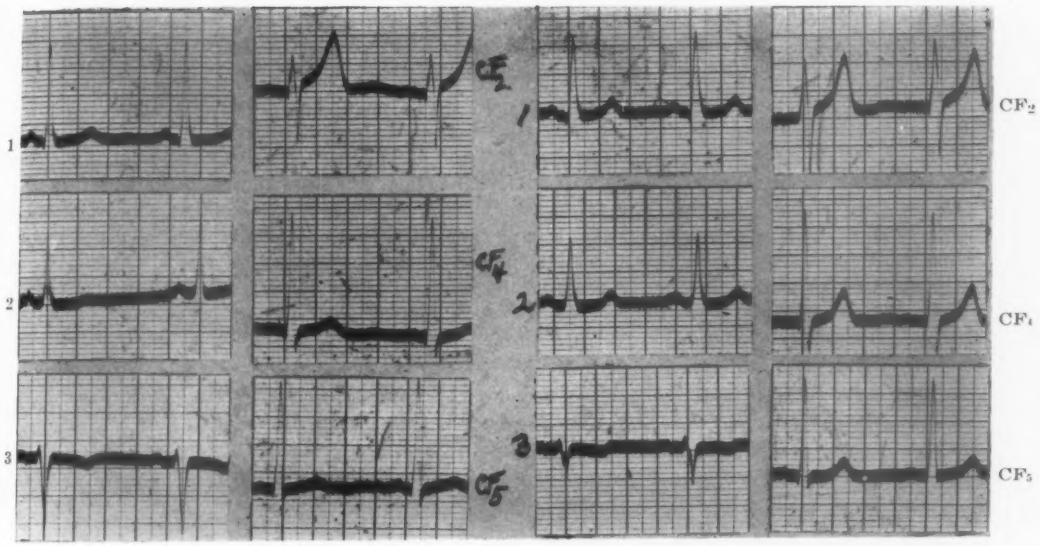
Fig. 10.—B. K., a woman, aged 27 years. *A*, Electrocardiogram taken Dec. 13, 1943; blood pressure, 220/100. *B*, Taken Jan. 14, 1944; blood pressure, 180/110. Sympathectomy Dec. 18 and 29, 1943.

CASE 11.—H. Z., a 50-year-old farmer, entered the Massachusetts General Hospital April 7, 1944, because of headaches and hypertension dating back five years. His history otherwise revealed rheumatic fever twenty-eight years before, hemorrhage from a gastric ulcer in 1939, and renal colic during the past year. There were no cardiac symptoms.

Physical examination showed no abnormalities except for hypertension (230/170), slight cardiac enlargement, and a slight apical systolic murmur. Ophthalmoscopic examination revealed Grade 2 hypertensive fundi. X-ray study showed slight enlargement of the heart, tortuous calcified aorta, clear lungs, and a normal pyelogram. An electrocardiogram (Fig. 11, *A*) taken April 10, 1944, showed normal rhythm (rate 70), slight to moderate left axis deviation, upright T waves in Lead I, almost flat T waves in Lead II, and low but upright T waves in Leads CF_4 and CF_5. The blood and urine were normal. Serum nonprotein nitrogen was 28.5 mg. per cent. The renal function (phenolsulfonphthalein) test registered 65 per cent in one hour.

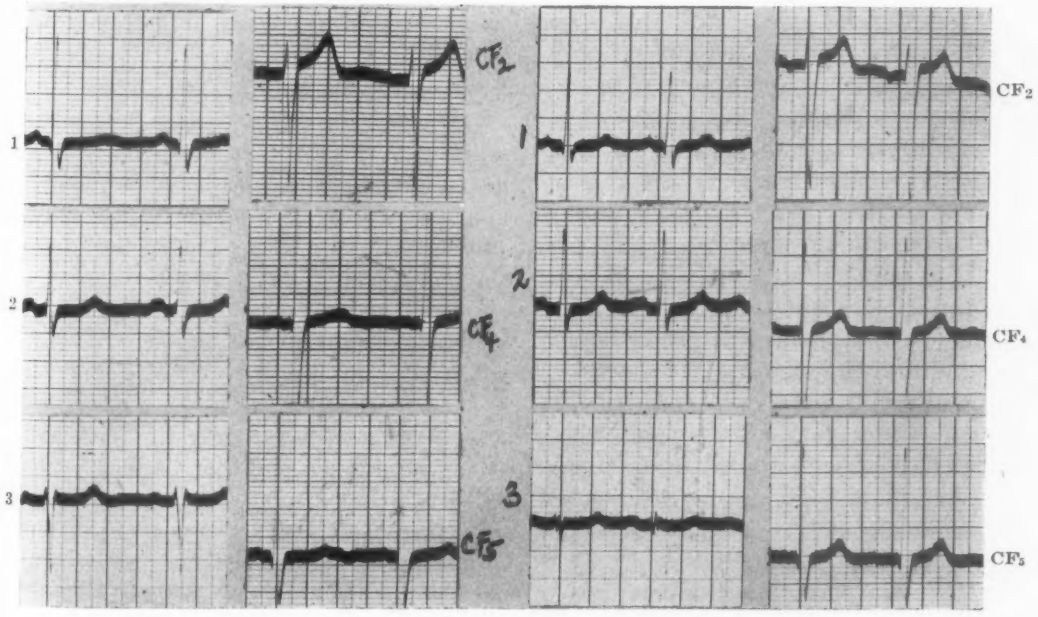
Lumbodorsal sympathectomy was carried out April 12 and 22, and the patient was discharged May 10 with a blood pressure measurement of 160/90. An electrocardiogram (Fig. 11, *B*) taken May 9, when the blood pressure registered 160/100, showed normal rhythm (rate 70), very little left axis deviation, and normal T waves in all six leads—a distinct improvement over the preoperative record.

CASE 12.—E. V. H., a 44-year-old male physician, entered the Massachusetts General Hospital Aug. 1, 1944, for study and treatment of hypertension of three years' duration. His blood pressure, previously normal, was found to register 165, systolic, and 120 to 130, diastolic, in 1941, when he was examined because of the onset of headaches. Since that time



A. *B.*

Fig. 11.—H. Z., a man, aged 50 years. *A*, Electrocardiogram taken April 10, 1944; blood pressure, 225/130. *B*, Taken May 9, 1944; blood pressure, 160/100. Sympathectomy April 12 and 22, 1944.



A. *B.*

Fig. 12.—E. V. H., a man, aged 44 years. *A*, Electrocardiogram taken Aug. 2, 1944; blood pressure, 210/130. *B*, Taken Aug. 30, 1944; blood pressure, 160/105. Sympathectomy Aug. 8 and 18, 1944.

the pressure had increased, with a high point of 250/165. There had been two brief episodes (lasting a few days) of numbness and tingling of the right arm and leg, disturbance of speech, blurring of vision, and difficulty in locomotion, which cleared without any sequelae. His headaches continued. He had stopped work in January, 1944. His past history was uneventful except for bilateral renal stones dating back sixteen years. There had been no cardiac symptoms.

On admission, his physical examination showed no important abnormalities except for a blood pressure of 210/130. The ophthalmoscopic examination showed Grade 2 hypertensive fundi. X-ray examination showed heart size and aortic shadow within the normal range, and small bilateral renal calculi. The electrocardiogram (Fig. 12, *A*) on August 2 showed normal rhythm (rate 70), slight to moderate left axis deviation, very low T waves in Lead I, and high R waves and very low T waves in Leads CF_4 and CF_5. The blood was normal. The urine showed a constant slight albuminuria with highest specific gravity (concentration test) at 1.015, occasional hyaline casts, and a few red and white blood cells. Renal function (phenolsulfonphthalein) test showed readings of 20 and 43 per cent in one hour. The blood nonprotein nitrogen was 24 mg. per cent.

Bilateral lumbodorsal sympathectomy was carried out on August 8 and 18. There were no complications. He was discharged from the hospital September 6. The blood pressure on September 5 measured 165/110. The electrocardiogram (Fig. 12, *B*) on August 30, twelve days after the second stage of the sympathectomy, when his blood pressure was 160/105, showed normal rhythm (rate 90), with normal axis and normal T waves in all six leads (I, II, III, CF_2, CF_4, and CF_5)—an improvement over the preoperative record.

DISCUSSION

This study was made not only to determine what alterations occurred in the electrocardiogram after adequate splanchnic resection but to correlate these alterations with other changes occurring in hypertension before and after operation so that the electrocardiogram could be utilized as an aid in the prediction of results to be obtained from surgery.

As previously stated, improvement in the electrocardiogram following various operations for hypertension has been mentioned several times.[1-5] Peet and co-workers[4] were the only ones to give any statistical data. They found the electrocardiogram to be improved in 53 per cent of 127 patients. Barnes[1] showed serial postoperative tracings of a patient who made an excellent recovery. None of the observers gave criteria for improvement, and none made any correlations. We believed that criteria should be set up upon which future comparisons could be made and by which minor changes, such as those associated with unimportant variations in heart rate,[7] occurring in any electrocardiogram could be eliminated. That we utilized minimal criteria on only five occasions should be emphasized. The preoperative and postoperative tracings were always taken in the same positions, since changes in position have been shown to affect the form of the electrocardiogram.[10]

Criticism could be made that our statistics are based only on patients upon whom postoperative electrocardiograms were taken and that patients who died during the same period should have been included to give a truer picture. So far as we were able to ascertain, only thirteen of the 209 patients selected for study of the limb leads had died when this report was made. Assuming that the same mortality rate obtained in the group upon whom follow-up electrocardiograms were taken, our statistics would have been affected adversely by only 5.4 per cent. It is true, of course, that a number of the graphs included in the tables presented contain too few individuals to be statistically significant, but it is of some interest to present them as we have found them for comparison with future data when many more cases are available for analysis.

Concerning correlations made with the postoperative electrocardiogram, there are several points of interest. The fact that chances for improvement in the electrocardiogram increased as the preoperative eye-ground picture became

worse is important since the prognosis in medically treated series becomes worse as eye-ground changes become more marked.[11] One would expect the electrocardiogram to be worse in patients with the more striking renal changes; therefore, the lack of such correlation in our cases is of significance. The absence of definite positive correlation between the postoperative electrocardiogram and the preoperative heart size, the patient's age, and the known duration of hypertension can be partially accounted for by the lack of definite positive correlation between these and the electrocardiogram before operation.[7] It is important, however, that chances for improvement in the electrocardiogram were not decreased in those with enlarged hearts, in those with a long-standing history of hypertension, or in those in the upper age brackets.

It is difficult to obtain a reliable diastolic blood pressure with which comparisons may be made since there are so many variables: the general state of the patient, the attitude, the acuity of hearing of the person taking the pressure, and the position of the patient. Despite inaccuracies, we believe that definite positive and negative correlations between postoperative electrocardiographic changes and preoperative or postoperative diastolic pressures are of considerable value. The greater incidence of improvement in the electrocardiograms of the patients with higher preoperative diastolic pressures is encouraging since it is in this group that relief of strain on the heart is most important. The symptoms of chest pain and dyspnea may be misleading unless they are carefully evaluated (both may be due to causes unrelated to hypertension or myocardial or coronary insufficiency). Nevertheless, they were included in our series of correlations, as were Q and T waves, in order to determine their value in deciding the advisability of operation in a given individual. Believing that it was important that improvement have duration, changes in the electrocardiogram were correlated with the length of time after operation at which they were taken. The changes in electrocardiograms taken later than six months after sympathectomy were important from another viewpoint—they represented specific results of splanchnic resection since nonspecific effects of operation doubtless had disappeared by this time. A further report will be made in the future of follow-up studies along this line.

The follow-up study of hypertensive patients on whom precordial leads have been done has to date been too brief for adequate appraisal of the changes in them since the majority of the electrocardiograms in this group were taken less than a month after sympathectomy, since nonspecific effects of the operation cannot be ruled out, and since a follow-up study six months or a year after operation will be needed to confirm the present evidence of improvement. However, in spite of that fact and the present difficulties in obtaining a series of precordial leads which are accurately placed, the evidence that improvement does occur seems incontrovertible. In electrocardiography the only comparable reversals in the precordial T waves that are well recognized at present occur with recovery from acute pericarditis, evolution of and recovery from myocardial infarction, and improvement after coronary insufficiency. Although the evolution of the precordial leads has not yet been adequately followed up in the case of hypertensive patients who have not been subjected to lumbodorsal sympathectomy for us to state definitely that such striking changes do not ever occur in them, no such improvement has been noted in those on whom we have obtained serial records to date. A careful long-term study of such cases is needed.

To explain these changes of the T waves toward the normal we shall probably have to know more about the physiologic effects of sympathectomy and also more about the actual mechanism of formation of the T wave itself. From this series we can conclude that definite changes toward the normal do occur

in the T waves of the precordial leads in a considerable percentage of hypertensive patients after lumbodorsal sympathectomy and that these evidences of improvement probably mean a lightening of the load (strain) on the left ventricle, a perfectly plausible effect of the reduction of the blood pressure from excessively high levels.

SUMMARY AND CONCLUSIONS

A study has been made of the effect of lumbodorsal sympathectomy (Smithwick's technique) on the electrocardiograms of hypertensive patients. Two groups of cases were used, an earlier one for the limb leads and a later group for precordial Leads CF_2, CF_4, and CF_5 after they began to be taken routinely in the study of the hypertensive patient. Lead IV was considered inadequate for this statistical analysis because of its inaccuracies. Although the limb leads and the multiple precordial leads were studied in two different groups, the conclusions concerning the limb leads of the cases of the earlier series were evidently applicable to the limb leads of the cases of the later series which formed the basis of the precordial lead study. It was generally, though not always, true that the changes in Lead I paralleled those in Leads CF_4 and CF_5; the last named was probably the most sensitive of all.

A striking improvement in the electrocardiogram, both in the limb leads and in the precordial leads, has been found in many cases of hypertension after radical lumbodorsal sympathectomy, details of which follow.

There has remained to be carried out a similar study of the evolution of the electrocardiogram in hypertension without the specific lumbodorsal splanchnic resection and a report concerning this follows in the third paper of the present series.

A. Limb-Lead Electrocardiograms.—Two hundred nine consecutive patients upon whom lumbodorsal sympathectomies were performed at the Massachusetts General Hospital were selected for study of the limb-lead electrocardiogram. Eighty-seven postoperative electrocardiograms were compared with those taken before operation on seventy-four patients whose records were abnormal to start with.

Postoperative electrocardiographic changes (changes in the T wave in Lead I, the electrical axis, and electrocardiogram as a whole) were correlated with preoperative eye-ground findings, heart size by teleroentgenogram, symptoms (dyspnea and chest pain), and the diastolic blood pressure on admission. They were also correlated with pathologic findings in renal biopsies, the length of time after operation at which the electrocardiograms were taken, and improvement in the diastolic blood pressure later than six months after splanchnic resection. Improvement in the T wave in Lead I was correlated with the degree of abnormality of the T wave before sympathectomy.

Criteria for improvement were established by which most minor nonspecific changes in the electrocardiograms were eliminated from our statistics. Improvement or unfavorable change in the T wave in Lead I or the electrical axis meant an elevation or depression of at least 1 mm. in the T wave and a shift of at least 15 degrees in the axis. Referring to the electrocardiogram as a whole, improvement meant improvement in the T wave or axis with or without changes in the other, or considerable improvement in one with only slight unfavorable change in the other. Unfavorable change in the electrocardiogram meant undesirable change using the same standards.

From these analyses and correlations, our limb-lead findings were as follows:

1. Electrocardiographic manifestations of hypertensive heart disease were frequently reversible by adequate splanchnic resection.

2. When changes occurred in the RS-T junctions and segments, the shift occurred in the same direction as that of the T waves but to a lesser degree. The RS-T junction and RS-T segment changes sometimes were insignificant and difficult to measure.

3. Improvement in the T wave of Lead I consisted of an elevation of the T wave.

4. Associated with the improvement in the height of the T wave in Lead I, the most frequent alteration in Lead III was a lowering of the T wave. Many times an upright T wave in Lead III became inverted, as it should be normally in many individuals.

5. Less frequently, improvement in Lead III consisted of elevation of the T wave. This change occurred in cases in which the T wave had been depressed by the hypertension.

6. Improvement in the T wave in Lead I was more marked than that in Lead III; therefore, when a change was measurable in Lead II, it was in the same direction but usually to a lesser degree than that in Lead I.

7. When improvement consisted of elevation of the T waves in Lead III, as well as in Lead I, the predominant change was in Lead II.

8. According to our criteria, the T wave in Lead I improved in 47.1 per cent, became worse in 8.1 per cent, and remained unchanged in 44.8 per cent. The axis improved in 29.8 per cent, became worse (more to the left) in 12.7 per cent, and remained unchanged in 57.5 per cent. The electrocardiogram as a whole improved in 57.5 per cent, became worse in 12.7 per cent, and remained unchanged in 29.8 per cent.

9. As the preoperative eye-ground findings and diastolic blood pressure readings on admission became worse, chances for improvement in the electrocardiogram increased.

10. No positive correlation could be found between postoperative electrocardiographic findings and preoperative heart size, known duration of the hypertension, symptoms (dyspnea and chest pain), or the patient's age.

11. The presence of inverted T waves in Leads I, I and II, II and III, or I, II, and III preoperatively did not alter the operative or electrocardiographic prognosis unfavorably. They appear to be in themselves indications for surgery rather than contraindications.

12. The presence of abnormal Q waves in Lead III did not alter the prognosis adversely, but it is possible that abnormal Q waves in Lead I did so.

13. Improvement in the electrocardiogram is more or less permanent—the incidence of improvement or unfavorable change varied little with the length of time following operation.

14. Improvement in the electrocardiogram was associated with improvement of the diastolic blood pressure.

15. The deeper the inversion of the T wave in Lead I before operation, the greater was the chance for postoperative improvement in the electrocardiogram.

B. Precordial Leads of the Electrocardiogram.—Comparative studies have been made of the preoperative and early postoperative precordial electrocardiograms (Leads CF_2, CF_4, and CF_5) taken on forty-eight patients who have had the Smithwick lumbodorsal sympathectomy for hypertension. In three cases electrocardiograms taken approximately one year after operation were also available for comparative study.

There were no changes in the QRS complexes or S-T segments which could be considered significant or of help in evaluating improvement in the postoperative precordial electrocardiograms, but further follow-up of this point is necessary.

The results of studies of the T-wave changes were as follows:

1. There were no changes early postoperatively in twenty-five (52.1 per cent) of the tracings of the forty-eight cases studied.

2. In nineteen cases, or 39.6 per cent, there was definite improvement in the early postoperative precordial electrocardiograms.

a. There was definite improvement in the T waves in both Leads CF_4 and CF_5 in eleven cases.

i. In five cases there was a marked change toward the normal with either one or both of the T waves which had been inverted becoming upright.

ii. In two cases the T waves were less deeply inverted.

iii. In five cases there was an increase in amplitude of low T waves of from 1 to 5 millimeters.

b. There was definite improvement in the T wave in Lead CF_5 alone in eight cases.

i. In two cases there was marked improvement, inverted T waves becoming upright and of normal voltage.

ii. In six cases there was an increase in the low T wave voltage of from 0.5 to 1.5 millimeters.

There were three cases on which follow-up tracings were available a year after operation. In the first of these cases there was no appreciable change in the precordial leads twenty-three days postoperatively, but there was definite improvement one year later. In the second case there was no significant change either in the record taken twenty-eight days postoperatively or in the one taken one year postoperatively. In the third case there was a slight progressive change for the worse twelve days and one year after operation; a tracing taken three and one-half months afterward was normal. This patient, however, had definite angina pectoris which was occurring rather frequently, and her coronary insufficiency probably accounted for the changes. In compiling our statistics only the immediate postoperative records, however, were considered.

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THE ELECTROCARDIOGRAM IN HYPERTENSION

III. Electrocardiograms of Hypertensive Patients Followed for a Long Time Without Splanchnic Resection in Comparison With Those in Patients Who Had Had Splanchnic Resection

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MUCH has been written on electrocardiography in hypertension, as many papers and books can prove.[1-16] Modifications and abnormalities that occur in the QRS complex, as well as in the RS-T junction and RS-T segment, the T waves, and the electrical axis have been described and discussed.

But a new aspect of this interesting subject was presented before a meeting of the New England Heart Association over a year ago, by White, Smithwick, and associates.[17] Two hundred nine consecutive patients, upon whom lumbodorsal sympathectomies were performed at the Massachusetts General Hospital, were selected for study by these authors; eighty-seven postoperative limb lead electrocardiograms were compared with the seventy-four records taken before operation on seventy-four patients, and forty-eight precordial electrocardiograms on as many patients were compared before and after operation.

They studied, in particular, the changes produced in the T waves in Lead I, in the electrical axis, in multiple precordial leads, and in the electrocardiogram as a whole. From this analysis they concluded as follows: "A striking improvement in the electrocardiogram, both in the limb leads and in the precordial leads, has been found in many cases of hypertension after radical lumbodorsal sympathectomy," and "There has remained to be carried out a similar study of the evolution of the electrocardiogram in hypertension without the specific lumbodorsal splanchnic resection and a report concerning this follows in the third paper of the present series."

Having become interested in these electrocardiographic changes following splanchnic sympathectomy, we sought in vain for published reports of comparable and adequate control studies, that is, studies of the evolution of the hypertension electrocardiogram in patients without such operation. Hence, we have collected as many such data as we have as yet been able to find which were based on adequate criteria. This search has been difficult and has yielded only fifty cases.

We obtained part of our material from the private files of one of us (P. D. W.) and from the records of the Massachusetts General Hospital. We were able to complete our control group through the kindness of the Heart Station of the Boston City Hospital, and Drs. Samuel A. Levine, James P. O'Hare, and Louis Wolff, to whom we are particularly indebted because they put at our complete disposal their own files of hypertensive patients' records and electrocardiograms and those of the Hypertension and Renal Clinics of the Peter Bent Brigham Hospital and of the Beth Israel Hospital, respectively.

We shall herewith compare the spontaneous evolution of the electrocardiograms of hypertensive patients with the changes already observed and pointed

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out on the electrocardiograms of patients upon whom Dr. Reginald H. Smithwick performed lumbodorsal splanchnic resection, using the same criteria presented by White, Smithwick, Mathews, and Evans.

At the very beginning, our criteria for selection of the control group of hypertensive patients were:

1. Age: under 50 years when first seen.
2. Duration of follow-up: at least five years.
3. No other kind of heart disease present at the start or later.
4. At least three electrocardiograms.

Because these conditions were difficult to meet, we were forced to modify them a little. We stretched the age limit to 54 years (for six cases only) and selected some cases who had had only two electrocardiograms instead of three but who had had tracings taken over a period of five years or more. We went through several hundreds of records in order to get these final fifty cases, and we carefully reviewed their corresponding records and electrocardiograms (240 tracings). In some of the cases the routine precordial Lead IVF was included in the follow-up study, but in none were multiple precordial leads obtainable for comparison since such leads have only recently been introduced for routine use.

Our control series was composed of thirty-four women and sixteen men.

The average age of the patients when first seen was 41 years and 8 months, and the average duration of follow-up was eight years and four months (range: five to twenty-one years). If we take into consideration this last figure, it becomes easy to see why we were unable to include in our series several cases with very high and long-standing blood pressure levels or with malignant hypertension. We know how quickly, at times, the evolution of such cases leads to death.

Following the new criteria for the selection of cases, we divided our patients into two groups according to their age:

Group 1: Patients less than 50 years of age.

Group 2: Patients more than 50 years of age.

The first group was, by far, larger than the second and consisted of forty-four cases out of the total of fifty; twenty-nine were females and fifteen were males. Five females and one male were included in the second group.

TABLE I

GROUP	TOTAL	FEMALES	MALES
1	44	29	15
2	6	5	1
	50	34	16

TABLE II. "SPONTANEOUS" EVOLUTION OF THE ELECTROCARDIOGRAM IN HYPERTENSION

	CASES	%
Questionable to slight improvement	5	10
Unchanged	20	40
Worse	25	50

TABLE III. GROUP 1; PATIENTS UNDER 50 YEARS OF AGE

	NUMBER OF CASES	IMPROVED	UNCHANGED	WORSE
Females	29	5	14	10
Males	15	–	6	9
	44	5	20	19

After a careful study of these fifty cases we arrived at findings expressed in Tables II and III.

Table III shows that the five improved cases were females. We found that the improvement was slight, at the most, in three instances and only questionable in the other two. Let us present these five cases in brief and see which have shown improvement in the electrocardiogram.

CASE 1.—M. E. was 34 years of age at onset of follow-up study. Duration of follow-up was twenty-one years. Seven electrocardiograms were taken during the period of observation. The first tracing showed T_1 to be positive (+1.5 mm.) and the S-T segments isoelectric; the blood pressure at that time measured 172/98. In the last electrocardiogram T_1 was positive but higher (+3 mm.) than in the first record. The S-T segment remained isoelectric, and the axis was unchanged (+50 degrees). No electrocardiographic changes were detectable in the other five tracings. The heart size remained within normal limits during the first ten years. The eye grounds were normal at the first two examinations; there was only a very mild vascular sclerosis at the time of the last ophthalmoscopic examination. The patient was always essentially asymptomatic.

CASE 2.—M. G., 41 years of age, was followed for five years. The first tracing showed depression of the S-T segments in Lead I (+1.5 mm.), inversion of the T waves in Leads I (-3 mm.) and II, and elevated S-T segments in Lead III, with an axis angle of -11 degrees. The blood pressure measurement was 225/140. A second electrocardiogram taken five years later showed that the S-T segments in both Leads I and II had become isoelectric, that T_1 was less negative (-1 mm.), and that T_3 was now positive. The electrical axis had shifted, however, more to the left (-22 degrees). The patient was never under digitalis therapy.

CASE 3.—A. J., 48 years of age. Duration of follow-up was eight years. Six electrocardiograms were taken. In the first of them, the T waves in Lead I were positive (2 mm.). The blood pressure readings were 180/100. In the last tracing T_1 had become higher (3 mm.) and the electrical axis had shifted from +25 to +59 degrees; the blood pressure at that time was 210/110. The heart showed the typical picture of left ventricular enlargement on fluoroscopy.

CASE 4.—G. McN., 49 years of age, was observed for five years. There was a questionable improvement of the electrocardiogram in this case. In the first tracing the S-T segments in Lead I were slightly depressed but became isoelectric later. The electrical axis remained unchanged, and the blood pressure readings were always around 175/110.

CASE 5.—A. B., 42 years of age, was followed for nineteen years. There was a question of slight improvement in this case. Three electrocardiograms were taken. The S-T segments in Lead I, at first depressed, became isoelectric and T_1 appeared to be more inverted in the first and second tracings than in the last. The electrical axis became more negative (from -36 to -58 degrees). The blood pressure rose from 160/110 to 210/120.

Of the remaining thirty-nine cases in this group, the electrocardiogram was unchanged in twenty and became worse in nineteen.

TABLE IV. GROUP 2; PATIENTS AGED 50 TO 54 YEARS

	NUMBER OF CASES	IMPROVED	UNCHANGED	WORSE
Females	5	-	3	2
Males	1	-	-	1
Total	6	-	3	3

A striking point in the entire series (both groups) was the lack of improvement.

DISCUSSION

The percentage of hypertensive cases showing any improvements at all in the present electrocardiographic study during a period of several years is decidedly low. We should add that this improvement is but slight or even but questionable, at times, as can be seen from the analysis of the five cases in which any possible change for the better was found.

Our study revealed the fact that the spontaneous evolution of the electrocardiograms of hypertensive patients is unfavorable in 50 per cent of the cases followed for some years, with no change in 40 per cent more. It would seem probable that a longer follow-up would show still more deterioration.

This shift from normal to more or less abnormal tracings depends in part on the length of time elapsed since hypertension appeared but chiefly on the levels reached by the blood pressure. In other words, the electrocardiogram has more chance of getting worse and worse when the blood pressure readings become higher and higher (especially the diastolic) as time goes on.

We have been told by others of the spontaneous improvement of the electrocardiogram in occasional cases, but from our recent experience we suspect that such instances are decidedly unusual or are to be ascribed to a complication, in particular, recovery from coronary insufficiency.

The age of the patient seems also to influence, in part at least, the ulterior course of the electrocardiogram. The older the patient the more chance for his serial tracings to become worse with the progression of time and with a long-standing hypertension. The younger patients are likely to stand high blood pressure better than do the aged. This is not always true, however, because some cases do show, in a relatively early stage of hypertension, strikingly unfavorable changes although the blood pressure is not alarmingly high, in contradistinction to other cases which stand a very marked rise of blood pressure for a long period without any appreciable electrocardiographic change. Let us now present in brief a case which illustrates this resistance.

CASE 6.—J. W., 24 years of age, sought medical advice because of headaches and pain in the back of her neck of six months' duration. At that time the heart was not enlarged by clinical examination, but fluoroscopy showed a moderate prominence of the left ventricle and a marked tortuosity of the aorta. A faint apical systolic murmur was present, and the aortic second sound was accentuated and louder than the pulmonary second sound. The blood pressure was 190/150. The eye-ground examination showed the arteries to be moderately narrowed in caliber and pale in color; a slight degree of a-v nicking was also present. The electrocardiogram was quite normal (T_1 upright and 3 mm. high, T_3 slightly inverted, S-T segments isoelectric, axis angle 42 degrees). The patient was followed for eight years. During this interval the blood pressure remained always high, but especially the diastolic, reaching 180 on several occasions. An x-ray film taken at the time of the last examination showed the heart size to be just above normal limits, and the electrocardiogram was almost superimposable on the tracing taken eight years before (T_1 upright and +1.5 mm. high, T_3 slightly inverted, axis angle 38 degrees).

Why do some persons stand very high blood pressure for a long period (Case 1) without having any symptoms at all and without showing unfavorable electrocardiographic changes, while other persons do not? Would it be possible to explain this fact on the basis of the existence of an individual or familial factor?

Let us look at Tables III and IV and note that we failed to find any favorable electrocardiographic change in our hypertensive men. Although we recognize the difficulties in establishing an adequate comparison between such small and unlike numbers (thirty-four women and sixteen men), one has the impression that the unfavorable evolution of the electrocardiogram in hypertensive patients is more frequent in men than in women. In only six of the sixteen men studied did we fail to find unfavorable changes in the tracings.

This comparison of the different evolutions of the electrocardiogram in hypertension in men and in women is in keeping with a concept already well accepted in cardiology, namely, that the clinical evolution and prognosis of hypertension in women seem to be definitely better than in men.

TABLE V. ELECTROCARDIOGRAMS (LIMB-LEADS)

	SERIES OF CASES SUBJECTED TO LUMBO-DORSAL SYMPATHECTOMY	%	PRESENT (CONTROL) SERIES	%
Improved	50	57.5	5	10
Same	26	29.8	20	40
Became worse	11	12.7	25	50
	87	100.0	50	100

And, finally, let us compare our results with those obtained by White, Smithwick, Mathews, and Evans after lumbodorsal sympathectomy.

As one can readily see, there is a striking difference between the spontaneous evolution of the electrocardiogram in hypertensive patients and the changes which develop after lumbodorsal splanchnic resection. The last word has, however, not yet been said. We must await the judgment of time.

SUMMARY AND CONCLUSIONS

1. We have compared the electrocardiograms of hypertensive cases followed for a long time with those of patients who have had Smithwick's lumbodorsal splanchnic resection for hypertension.

2. Our control series consisted of fifty cases, forty-four of whom were less than 50 years of age when first seen; six were a few years older (from 50 to 54 years of age). There were thirty-four women and sixteen men in this group. A total of 240 electrocardiograms belonging to the fifty cases were studied.

3. The average age of these fifty patients when first seen was 41 years and 8 months, and the average follow-up period was eight years and four months (range: five to twenty-one years). No other kind of heart disease was present either at the start or later on during the evolution of the hypertension.

4. The fifty patients were divided into two groups according to age; forty-four patients less than 50 years old comprised the first group, twenty-nine of whom were females and fifteen males. Only six patients were included in the second group and their ages varied between 50 and 54 years.

5. The electrocardiograms of only five out of the fifty cases showed any possible improvement at all, and then it was questionable or slight. The serial tracings of twenty patients (40 per cent) failed to show any appreciable modification. Those of twenty-five cases (50 per cent) had an unfavorable electrocardiographic evolution.

6. All of the improved cases were women less than 50 years of age when the follow-up study began.

7. No favorable changes were detected among the male patients, or in the group of patients older than 50 years.

8. In accord with these facts, one may conclude that the electrocardiogram in hypertension tends to become worse as time goes on and that there exists a definite parallelism between the clinical course and the electrocardiographic evolution of this disease. Age, sex, and especially the passage of time appear to act unfavorably in the evolution of the hypertensive electrocardiogram.

9. There is a striking difference between the spontaneous evolution of the hypertensive electrocardiogram and the picture which develops after lumbodorsal sympathectomy markedly in favor of the latter.

10. A longer period of time must elapse, however, before final judgment can be passed concerning sustained improvement of the hypertensive electrocardiogram after lumbodorsal sympathectomy.

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CLINICAL OBSERVATIONS WITH CERBERIN

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THIS publication is for the purpose of describing the first use of cerberin on human subjects.

Cerberin is a glycoside which has been extracted from the kernel of *Cerbera odollam*, a tree native of India, Dutch East Indies, and certain islands of the Southwestern Pacific. DeVry,[1] in 1864, was first to discover that the expressed oil of the kernels of this tree contained a substance which had a digitalis-like action. In 1893, Plugge[2] found that this substance would cause systolic standstill of the frog's ventricle. More recently, Chen[3] became interested in *Cerbera odollam*. His intent was to isolate cerberin and other active substances which might be present in the kernels of the nuts and to conduct various pharmacologic experiments with these pure principles. He standardized the drug according to

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the method used for digitalis. After this was done, it was at his suggestion that the following clinical work was carried out.

METHODS

It was decided that the effect of cerberin could best be demonstrated in patients with auricular fibrillation. Patients were selected who had received no previous digitalis medication and who were in sufficiently good condition to make the use of diuretics unnecessary. This was not always possible.

Upon admission each patient was given complete rest in bed, with sedation of necessary, for eighteen to twenty-four hours, and in two cases as much as ten days' rest in bed was maintained before medication was begun. This was done to discount the effects of rest upon the fibrillation before cerberin was given.

The course of the patient was followed by electrocardiograms, venous pressure by the direct method,[4] vital capacity,[5] chest plates, and a careful check, twice daily, of the apical and radial rates. Where the condition of the patient made it possible, circulation times were done. For this the procedure was:

Four minims of ether were injected into the antecubital vein for the arm-to-lung time[6] and 4 to 6 c.c. of 20 per cent neocalglucon were used for the arm-to-tongue test.[7]

In the first ten cases cerberin was given intravenously as we were not familiar with its rate of absorption from the intestinal tract. In the last five cases an oral preparation was used. In each instance 1 c.c. of the solution equaled 2½ cat units. Since this is the first clinical use of cerberin, we had to proceed cautiously in its administration. Therefore, in the beginning, we decided not to give more than 5 cat units per day intravenously. When the oral preparation was used, it was given in sufficient doses to slow the apex rate to the desired level and reduce the pulse deficit to a minimum.

RESULTS AND DISCUSSION

Cerberin was administered to fifteen patients, fourteen of whom had auricular fibrillation and one of whom was in congestive failure with a regular rhythm. These fifteen patients were classified as follows: Four with the diagnosis of rheumatic heart disease, two with the diagnosis of hypertensive heart disease, seven with the diagnosis of arteriosclerotic heart disease, and two with the diagnosis of thyrotoxicosis.

In one case the fibrillation ceased before the effect of the drug could be determined. In two instances the fibrillation was controlled and the patients carried through surgery: one a thyroidectomy, the other a leg amputation.

The following two case histories are representative of our methods and the actions of this drug.

Mrs. O. Z., R.N. and housewife, aged 51 years, was first seen on January 14. Her complaint at that time was "blood clot in right leg."

Present Illness.—On January 4, the patient developed a severe cold. The cold gradually improved, and no cardiac complaints could be elicited. On January 12 she developed a sudden pain in the right leg followed by coldness, numbness, and loss of function of the leg. By the next day definite purplish discoloration of the foot had occurred. This progressed to involve the distal two-thirds of the right leg by the time of admission.

Past History.—Significant points in the past history were: (1) Systolic blood pressure of 180 was found at age of 21 years while she was being examined for a "strained heart." (2) In 1935 she had a mild "heart attack" and was in bed for six months. (3) She had a stroke in 1937 which resulted in paralysis of the right side of the face, right arm, and right leg and aphasia which has gradually improved since that time. No definite rheumatic history could be elicited. Family history was negative.

Physical Examination.—The patient was in a fairly good condition. She showed a mild speech defect. The ocular fundi showed tortuous arteries with notching at the arteriovenous crossings. The lung fields were clear. There was slight enlargement of the heart on physical examination. There was a rapid fibrillation with an apex rate of 165 to 170 and a radial rate of about 80. No definite signs of congestive heart failure were found. Blood pressure was 160/110.

There was a purplish discoloration of the right foot and the distal two-thirds of the right leg. The foot was cold, and no dorsalis pedis pulse was palpable.

Laboratory.—Urine and blood findings were normal. Total nonprotein nitrogen was 28 mg. per cent. Clotting time was three minutes; bleeding time, one minute. Serology was negative. Electrocardiogram showed auricular fibrillation with ventricular rate of 165 per minute.

X-Ray.—X-ray of the chest showed no definite signs of congestive failure; it showed enlargement of the heart with accentuation of left auricular curve and a suggestion of mitral stenosis.

Diagnosis.—The diagnosis was arterial hypertension and possible rheumatic heart disease with mitral involvement, auricular fibrillation, and embolus in right popliteal artery with early gangrene of right leg.

Course and Treatment.—The patient was kept at rest in bed, and given mild sedation with phenobarbital and codeine. The fibrillation was controlled with cerberin. Venous pressure on admission was 8.5 cm. of water. Fifteen days later it was 7.5 cm. of water. Arm-to-lung time on admission was 8.2 seconds; fifteen days later it was 7.5 seconds. Arm-to-tongue time on admission was 22 seconds; fifteen days later it was 15 seconds. Vital capacity improved from 38 per cent at admission to 64 per cent at discharge. Electrocardiograms showed a gradual slowing of the ventricular rate from 165 per minute to 80 per minute.

Amputation of the right leg to 20 cm. above the knee joint was done on the seventh day of the patient's hospital stay with an uneventful recovery.

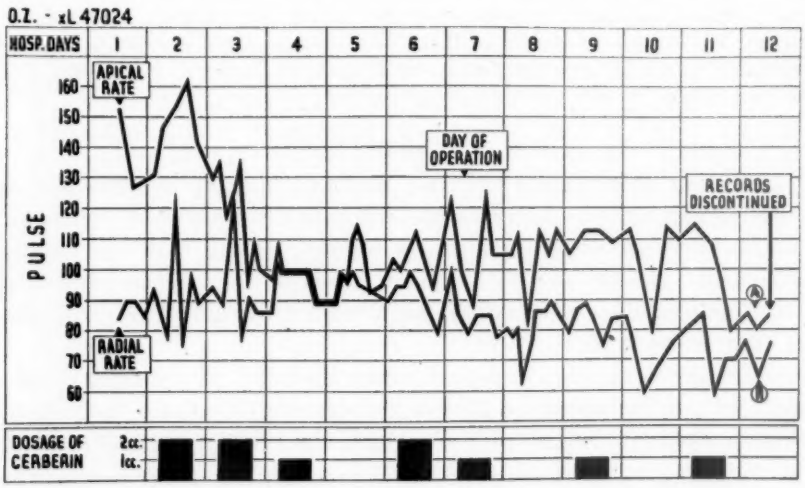

Fig. 1.

Fig. 1 shows the record of the apical and radial rates and the dosage of cerberin given. Fig. 2 shows the electrocardiogram on admission and after five days on the preparation.

CASE 2.—E. S., a white woman, aged 75 years. Her chief complaints were "heart fluttering" diabetes, and a cold right foot.

Present Illness.—Her ability to exercise had been greatly limited for the previous two to three years because of shortness of breath accompanied by irregularity of the heart. She had had mild swelling of the feet and ankles for the same period of time. Two weeks before admission she developed a sudden pain in the right foot which had since become blue and cold. She was known to have diabetes for the previous three years.

Physical Examination.—Positive findings: Eyes, moderate arteriovenous nicking with tortuosity of the arteries; slight orthopnea with overdistention of the jugular veins in the flat posture; lung fields, clear; heart, auricular fibrillation present, apex in fifth intercostal space about 1 cm. to the left of mid-clavicular line, blowing Grade 2 systolic murmur at mitral area; liver, not palpable; extremities, no edema, right foot blue and cold up to 3 inches above lateral malleolus, no arterial pulsation in this foot, but present in the left; walls of radial arteries felt thickened upon palpation.

Laboratory.—Urinalysis: heavy trace of albumin; 2 to 3 per cent sugar; 8 to 10 pus cells. Blood: hemoglobin, 13; white blood cells, 6,800 with normal differential. Blood sugar, 168 mg. per cent. Phenolsulfonphthalein test, 72 per cent in fifteen minutes.

DATE	TIME	VENOUS PRESSURE	CIRCULATION TIME (SEC.) ETHER	CALCIUM GLUCONATE	ECG
6/12/42	11:30 A.M.	15.5 to 16.0 cm. H_2O	18	39 to 32	+
6/17/42	5:00 P.M.				+
6/18/42	2:00 P.M.	8.5 to 9.0 cm. H_2O	10.0 to 5.0	23.5 to 11.0	
6/20/42	10:15 A.M.	8.0 cm. H_2O		22.0	

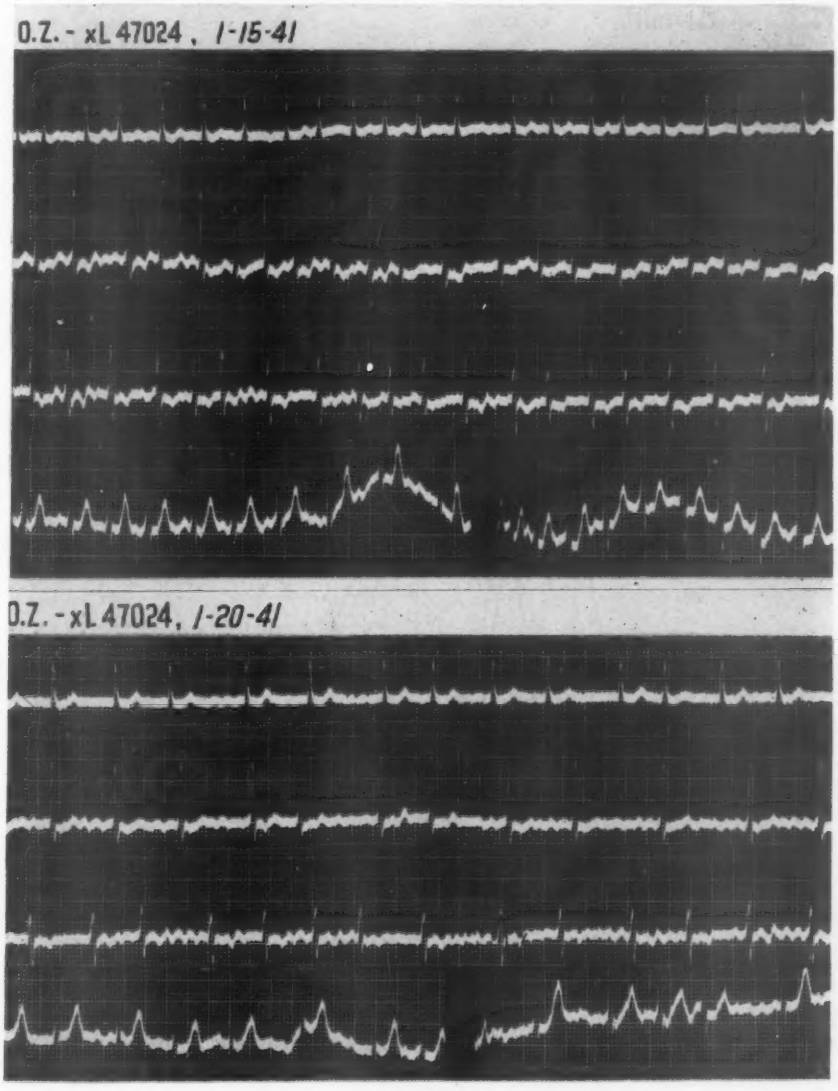

Fig. 2.

X-Ray.—X-ray showed definite cardiac enlargement.
Treatment.—The treatment consisted of rest in bed, sedatives, and cerberin.

Fig. 3 shows the record of apical and radial rates and dosage of cerberin. Fig. 4 shows the electrocardiogram on admission and after five days on the drug.

DISCUSSION AND RESULTS

Of the fifteen people who have received treatment with cerberin, in two instances it was found that no medication was necessary, and so the drug was discontinued. One patient was moribund on admission and died soon afterwards. In one patient with congestive failure and a regular heart rate no benefit was obtained from the use of cerberin. In this instance the drug was discontinued, the patient was digitalized, and mercurial diuretics were used. However, none of these measures resulted in conmplete compensation of the patient.

Of the remaining eleven patients, two had auricular fibrillation with no evidence of congestive failure. The remaining nine had auricular fibrillation and were in congestive failure, as confirmed by both clinical and laboratory findings. In six of these patients cardiac compensation resulted after the fibrillation had been controlled with cerberin and the patient kept at rest in bed with sedation. In three instances these measures were ineffectual, and diuretics were necessary in order to bring about compensation.

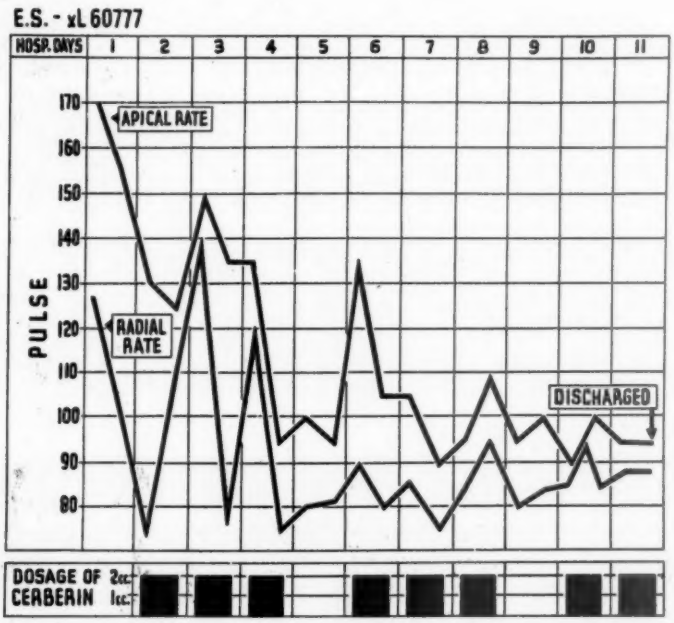

Fig. 3.

We do not intend to intimate that the control of fibrillation alone resulted in compensation in these cases. We do not know the complete action of cerberin, and in this paper we are dealing only with its effect on fibrillation.

It was noted that cerberin produced a slowing of the pulse much more quickly than did digitalis. One patient demonstrated this especially well. A woman with advanced mitral stenosis, intense cyanosis, orthopnea, cold, clammy extremities, an apical rate of 160 per minute, and a radial rate too feeble to count was given 10 cat units of cerberin intravenously. Within five minutes after injection, her pulse was reduced to 110 per minute with no pulse deficit, and there was a remarkable improvement in all symptoms noted above.

On the other hand it was noted that the effect was much more transitory than with digitalis. For example, in one case which had a very rapid fibrillation and had been controlled with cerberin, discontinuance of the drug resulted in a return of the pulse to a pre-medication level in thirty-six hours.

No untoward effects were noted with administration of cerberin except in one case. In this instance the patient's apical rate had been slowed by the drug to about 50 per minute, and he developed anorexia, nausea, vomiting, and abdominal cramps. The drug was stopped, and on the third day all symptoms had disappeared.

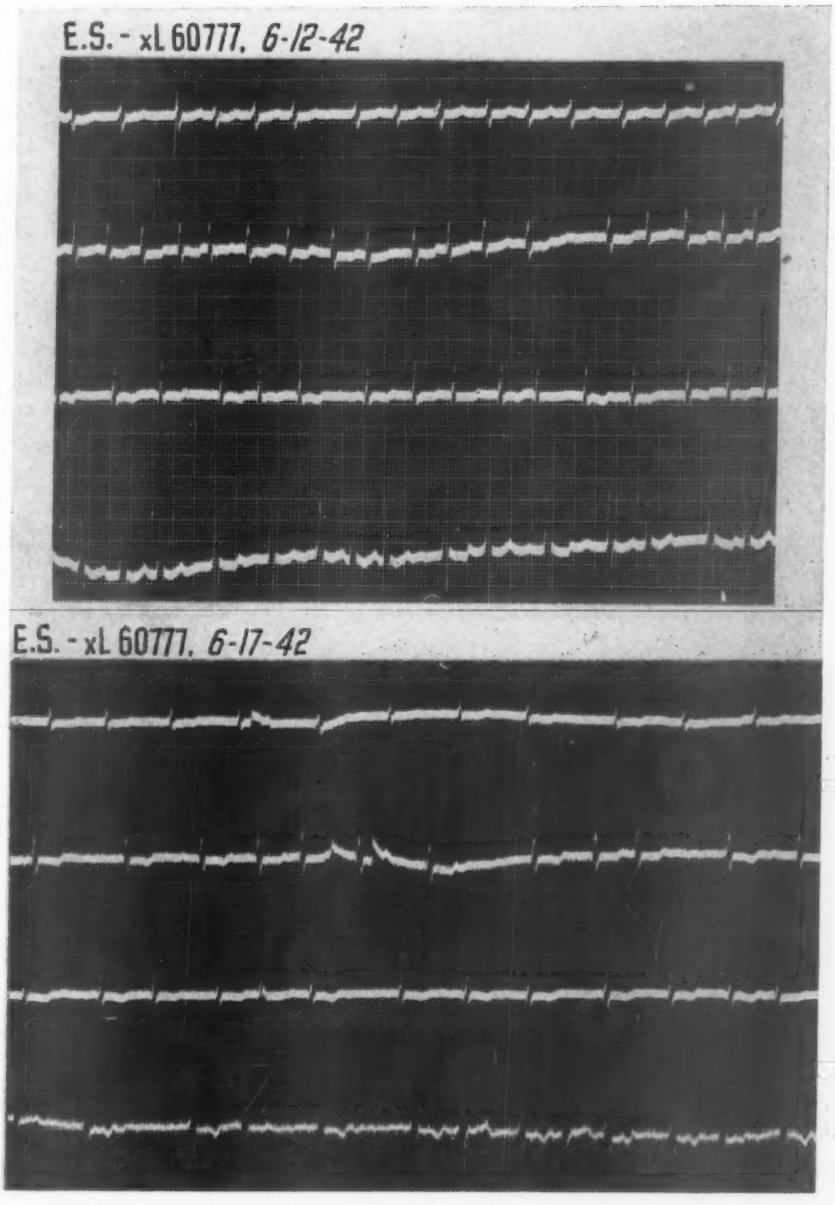

Fig. 4.

Table I is a summary of all the cases in which the drug was tried and the results obtained.

Since our series of cases is small and we had to proceed cautiously in the administration of the drug, we were not able to estimate the average dose necessary for control of auricular fibrillation.

TABLE I

NAME	AGE (YRS.)	DIAGNOSIS	DAYS ON DRUG	METHOD OF ADMINISTRATION	CIRCULATION TEST (ON ADMISSION)	CIRCULATION TEST (ON DISCHARGE)	COMMENT
L. K.	93	Arteriosclerotic heart disease with auricular fibrillation	28	Per os.	Unable to cooperate		No other medication necessary
M. M.	35	Rheumatic heart disease with auricular fibrillation	5	I.V.*	Ether = 20 seconds CaGlu.† = 53 seconds Ven.Pr.‡ = 26 cm. T_2O	Ether = 20 seconds CaGlu. = 37 seconds Ven.Pr. = 25 cm. H_2O	Ceased fibrillating. Drug discontinued
E. M.	58	Rheumatic heart disease. Auricular fibrillation. Decompensated	18	I.V.	Ether = 10 seconds CaGlu. = 22 seconds Ven.Pr. = 18.6 cm. H_2O	Ether = 7 seconds CaGlu. = 17 seconds Ven.Pr. = 12.6 cm. H_2O	No other medication necessary
N. P.	43	Rheumatic heart disease with auricular fibrillation. Slightly decompensated	40	Per os and I.V.	Ven.Pr. = 41 cm. H_2O Vit.Cap.§ = 33%	Ven.Pr. = 24 cm. H_2O Vit.Cap. = 39%	Diuretics necessary to compensate
O. Z.	51	Hypertensive heart disease with auricular fibrillation. Slightly decompensated	10	I.V.	Ether = 8.2 seconds CaGlu. = 22 seconds Ven.Pr. = 8 cm. H_2O	Ether = 7.5 seconds CaGlu. = 15 seconds Ven.Pr. = 7 cm. H_2O	No other medication necessary. Leg amputation
C. M.	50	Hypertensive heart disease with auricular fibrillation. Decompensated	17	IV.	Ether = 9.6 seconds CaGlu. = 25 seconds Vit.Cap. = 41% Ven.Pr. = 26.5 cm. H_2O	Ether = 5 seconds CaGlu. =12 seconds Vit.Cap. = 75% Ven.Pr. 12 cm. H_2O	Diuretics unnecessary
M. K.	53	Thyrotoxicosis with auricular fibrillation. Decompensated	39	I.V.	Ven.Pr. = 33 cm. H_2O Vit.Cap. = 34%	Ven.Pr. = 11 cm. H_2O Vit.Cap. = 58%	No other medication necessary. Thyroidectomy
C. S.	57	Arteriosclerotic heart disease with auricular fibrillation. Decompensated. Carcinoma of rectum	41	Per os	Excellent results Records lost		No other medication necessary
E. P.	47	Hypertensive heart disease with auricular fibrillation. Decompensated	8	Per os	Ven.Pr. = 20 cm. H_2O		Diuretics necessary
H. D.	32	Rheumatic heart disease. Not fibrillating. Decompensated	46	I.V.	Ven.Pr. = 23 cm. H_2O Vit.Cap. = 35%	Ven.Pr. = 12 cm. H_2O Vit.Cap. = 59%	Treatment unsatisfactory
C. K.	70	Arteriosclerotic heart disease with auricular fibrillation. Decompensated	13	I.V.	Ether = 15 seconds CaGlu. = 32 seconds Ven. Pr. = 16 cm. H_2O Vit.Cap. = 65%	Ether = 9 seconds CaGlu. = 16 seconds Ven.Pr. = 12 cm. H_2O Vit.Cap. = 75%	No other medication necessary
E. S.	75	Arteriosclerotic heart disease with auricular fibrillation. Decompensated		I.V.	Ether = 8 seconds CaGlu = 35 seconds Ven.Pr. = 15 cm. H_2O	Ether = 5 seconds CaGlu. = 22 seconds Ven.Pr. = 8 cm. H_2O	No other medication necessary
A. H.	70	Arteriosclerotic heart disease with auricular fibrillation. Decompensated	2	I.V.	Patient unable to cooperate		No medication necessary
A. H.	73	Arteriosclerotic heart disease with auricular fibrillation. Decompensated	39	Per os.	Ven.Pr. = 15 cm. H_2O	Ven.Pr. = 9.5 cm. H_2O	No other medication necessary
T. W.	58	Thyrotoxicosis with auricular fibrillation. Decompensated	3	Per os	Unable to cooperate		Treatment unsatisfactory. Patient died

*I.V. = intravenously.
†CaGlu. = calcium gluconate.
‡Ven.Pr. = venous pressure.
§Vit.Cap. = vital capacity.

We were interested in determining whether or not any electrocardiographic changes occurred during medication with this drug. Since we used the drug almost entirely on patients with auricular fibrillation, we were unable to determine if the drug produced any change in the P-R interval. In three instances, definite inversion of the T waves was noted. It has been found, however, that, in cats, when cerberin was given by slow perfusion up to the fatal dose and serial electrocardiograms were taken, definite cardiographic abnormalities occurred. The first change was a definite slowing of the rate. This was followed by a prolongation of the P-R interval. Complete A-V block followed this. With increasing doses, ventricular tachycardia occurred which changed to ventricular fibrillation resulting in the death of the animals.[3]

SUMMARY

1. Auricular fibrillation can be controlled satisfactorily with the intravenous or oral use of cerberin.

2. Cerberin exerts its effect on auricular fibrillation much more rapidly than does digitalis. Its effect is also more transitory after the drug is discontinued.

3. No untoward effects were noted when therapeutic doses of the drug were used.

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Clinical Reports

ANGINA PECTORIS ASSOCIATED WITH DEXTROCARDIA AND SITUS INVERSUS (CASE REPORT)

LIEUTENANT COLONEL J. C. CAIN, M.C.

DEXTROCARDIA with situs inversus has long been recognized by physicians. It is known to occur in approximately one out of 35,000 physical examinations of recruits for the United States Army.[1] These individuals usually lead a normal life unless they have some obvious organic, valvular, or myocardial defects. The present case is of interest primarily because of its rarity. The symptoms of angina pectoris are typical, except that distribution of the pain is primarily substernal to the right of the sternum and down the ulnar side of the right arm. This man was inducted into the Army and performed the regular Army duties for approximately one month. He was admitted to the hospital because of an infected right toe. During his stay at the hospital it was found that he had complete transposition of all the organs of the body and symptoms typical of angina pectoris. He was discharged from the Army because of angina pectoris and dextrocardia with situs inversus.

CASE HISTORY

A 33-year-old Russian Jewish man, entered the Station Hospital, Camp Gruber, Oklahoma, Aug. 23, 1942, complaining of an infected right large toe. This infection rapidly subsided. Dextrocardia was discovered in 1924, but no symptoms were present. In 1940, while helping to carry an object weighing approximately 275 pounds, his first attack of substernal distress occurred. The pain was described as being "severe, constricting, like a pressure, and squeezing" in nature. It was located in the mid-sternal region and just to the right of the sternum. The pain lasted only a few minutes. He was very frightened and "felt sure he was going to die." He "broke out in a cold clammy sweat," and the pain radiated down the ulnar side of the right arm as far as the tip of the fourth and fifth fingers. Following this he entered the King's County Hospital, in Brooklyn, N. Y., and was told that he had dextrocardia and angina pectoris. Electrocardiograms were taken and supposedly confirmed the diagnosis. Since that time he has had approximtely seven severe attacks and innumerable minor attacks. Following a severe attack he feels weak, frightened, and nauseated, but never vomits. For the following two or three days he is unable to do any work, but during this time he has no pains. The attacks are precipitated by fright, heavy lifting, exercise, emotion, intercourse, and walking into a cold wind. Attacks are more likely to occur after large meals. Prompt relief is obtained by stopping whatever he is doing and standing perfectly still or by taking 1/100 grain of nitroglycerin. The attacks never last more than five minutes.

The patient was a very excitable Jewish individual. He had done no heavy work and had lived on relief for the previous year and a half. He had frequent headaches, pyrosis, and dyspnea. He was very nervous, did not sleep well, and smoked approximately two packages of cigarettes a day. Tremor was marked. He bit his fingernails and had excessive sweating. The angina pectoris had become decidedly worse since he had been in the Army.

The family history was interesting in that his mother and three maternal uncles died suddenly from heart disease. Unfortunately, he did not know whether any of these relatives had dextrocardia. One brother was being treated for heart trouble, but the symptoms

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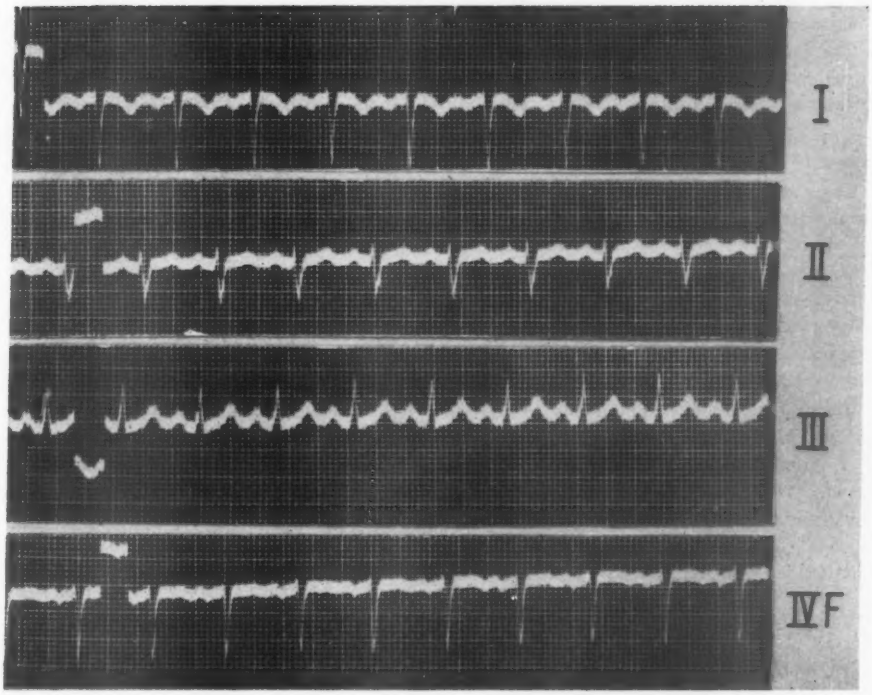

Fig. 1.—Electrocardiogram of dextrocardia showing the three standard leads and IVF. Rate 112; inversion of all complexes in Lead I, normal complexes in Lead II, and right ventricular preponderance. Lead IVF shows all complexes inverted.

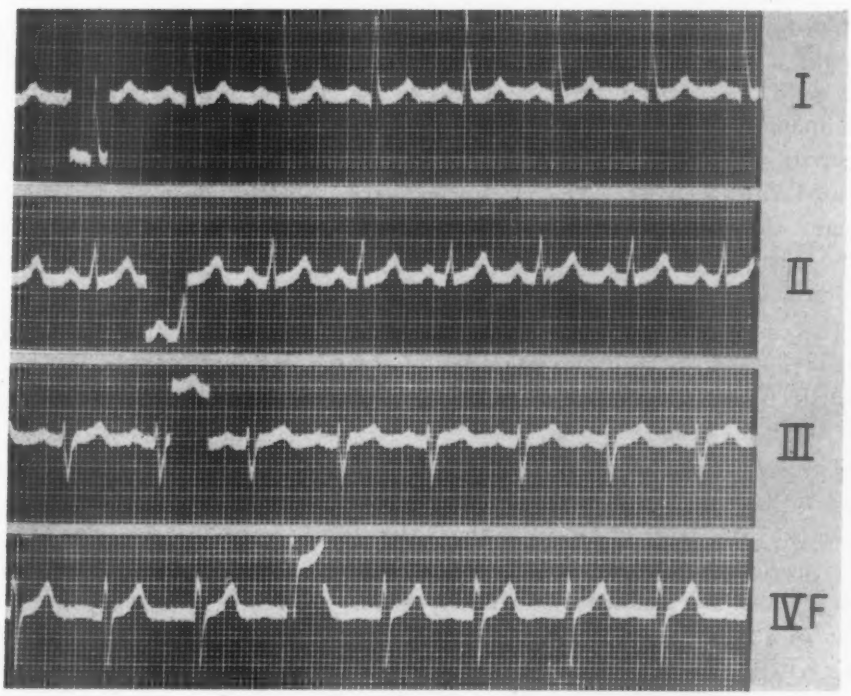

Fig. 2.—Electrocardiogram of dextrocardia after interchanging the arm wires; rate 92; all waves positive in Lead I. Lead II is the same as Lead III in Fig. 1. Lead IVF shows all complexes upright with a large S wave. This electrocardiogram shows left ventricular preponderance.

as described by the patient were highly suggestive of hysteria. The man's wife and three children were normal. The remainder of the family history was irrelevant.

The past history indicated that he had never been well or capable of participating in the usual activities of children. He had had vague joint pains, but no clear-cut history of rheumatic fever could be elicited. The only childhood disease was pertussis.

The physical examination revealed a stout, muscular individual, 5 feet, 6 inches tall, weighing 172 pounds. No gross physical defects were noted on inspection. The blood pressure was elevated, being 156/106. By percussion the heart was found to be in an unusual location with the apex located 9 cm. to the right of the mid-sternal line in the fifth intercostal space. The point of maximum intensity could easily be seen in the fifth intercostal space 9 cm. to the right of the mid-sternal line. A soft, blowing, nontransmitted systolic murmur was present in the region of the fifth intercostal space 9 cm. to the right of the mid-sternal line. The rate and rhythm of the heart were normal. Palpation of the abdomen revealed the tip of a mass in the left upper quadrant; percussion over this area suggested liver dullness. There was no evidence of a liver on the right side of the abdomen.

Roentgenographic examination of the chest and abdomen definitely showed dextrocardia and evidence of transposition of the liver, spleen, and stomach. The electrocardiogram, Fig. 1, disclosed that the rate was 112 beats per minute. All complexes in Lead I were inverted. The QRS of Lead II was downward and slurred. Lead III showed all complexes upright. By changing the arm electrodes, Fig. 2, a normal electrocardiogram, was produced. The QRS complex in Lead III was downward, and there was left ventricular preponderance. A diagnosis of dextrocardia and left ventricular preponderance was made.

COMMENT

Reports of dextrocardia associated with organic heart disease are quite rare. Willius[2] reported a case of dextrocardia with situs inversus complicated by hypertensive heart disease. Crawford and Warren[3] recently reported the first case of coronary thrombosis in a case of dextrocardia and situs inversus, and two months later a case of hypertension and coronary heart disease associated with this condition was described by Manchester and White.[4] It is interesting that in the case described by Crawford and Warren[3] the pain associated with the coronary thrombosis was to the right of the sternum, and there was numbness of the right arm. The pain often lasted as long as an hour and frequently occurred in the absence of exercise or other recognized causes of increased cardiac work. The electrocardiogram showed clear-cut evidence of coronary thrombosis. The patient in the case described by Manchester and White[4] complained of pain following exercise located just to the left of the sternum. There was no radiation of pain to the arms or neck.

The case described here represents the first report of typical true angina pectoris associated with dextrocardia and situs inversus. It is interesting primarily because of the radiation of the pain to the right of the sternum and down the right arm.

The exact cause of the pain of angina pectoris is unknown, but the etiology seems to be associated with coronary artery insufficiency and myocardial anoxemia. The pain fibers from the heart travel centrally over the cervical and thoracic sympathetic cardiac nerves to the white rami of the spinal nerves T_1 to T_4 and are classified as general visceral afferents. Since the heart develops as a midline structure and since it receives nerve fibers from both sides of the central nervous system, it is difficult to explain why most cases of angina pectoris have pain referred to the left side. The pain is occasionally referred bilaterally; it has been reported with reference chiefly to the right side, but the latter type is very unusual. This case seems to represent not only gross reversal of the organs but also reversal of the plan of innervation of the heart.

SUMMARY

A case of angina pectoris with pain radiating to the right arm is reported in an individual with dextrocardia with situs inversus.

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COMPLETE HEART BLOCK IN GERMAN MEASLES

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ARMY OF THE UNITED STATES

IT IS well known that auriculoventricular heart block may occur during the course of acute infections. Its frequency in rheumatic fever is generally recognized. It has been reported in such infections as diphtheria[1] influenza,[2] typhoid fever,[3] pneumonia, scarlet fever, and typhus fever.[4] Textbooks[5] mention endocarditis as a rare complication of German measles, and pericarditis, myocarditis, and endocarditis as complications of measles. The occurrence of heart block in German measles has not been reported so far as we are able to determine from a review of the literature of the past twenty-six years. The rarity of this condition prompts the present report.

REPORT OF CASE

A private, aged 23 years, was admitted to the hospital on March 24, 1943, complaining of sore throat and glandular swelling in the neck which had been present for three days. The past history revealed an attack of mumps during childhood. There was no history of rheumatic fever or chorea.

Physical examination showed a moderate pharyngitis with swelling of the posterial cervical glands, most marked on the left side. The heart was of normal size. No murmurs were heard. The rhythm was regular. The blood pressure was 110/68. The examination otherwise was essentially normal.

Laboratory examination revealed 23,100 white blood cells with a normal differential count. The Wassermann and Kahn reactions of the blood were negative. Four days after admission there were 18,000 white blood cells with 78 per cent polymorphonuclear leucocytes, 15 per cent lymphocytes, and 7 per cent monocytes. During the first two weeks in the hospital the temperature ranged from 100° F. to 101° F. and then returned to normal. Five days after admission the patient was given 22 Gm. of sulfadiazine extending over a period of four days without apparent beneficial effects. On the ninth hospital day the patient became dizzy and almost fainted in the lavatory. The pulse rate was 38. An electrocardiogram taken at this time revealed complete heart block (Fig. 1). A blood count showed 11,550 white blood cells with a normal differential count. On the tenth hospital day the pulse rate was 80, and partial heart block was present with a three-to-two rhythm (Fig. 2, *A*). Atropine sulfate, 0.00096 Gm., was given intravenously with an immediate decrease in the

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degree of block and the establishment of a one-to-one rhythm (Fig. 1, *B*). On the twelfth hospital day the P-R interval was 0.28 second (Fig. 2, *C*), and on the sixteenth hospital day it was 0.22 second. On the seventeenth and twenty-sixth hospital days (Fig. 2, *D*) the P-R interval was 0.21 and 0.16 second, respectively. On the fourteenth hospital day and five days after the onset of the complete heart block, the spleen became palpable and a generalized, pinkish, papular eruption appeared over the trunk and extremities, and to a lesser extent over the face. There were no Koplik's spots. Laboratory examination revealed

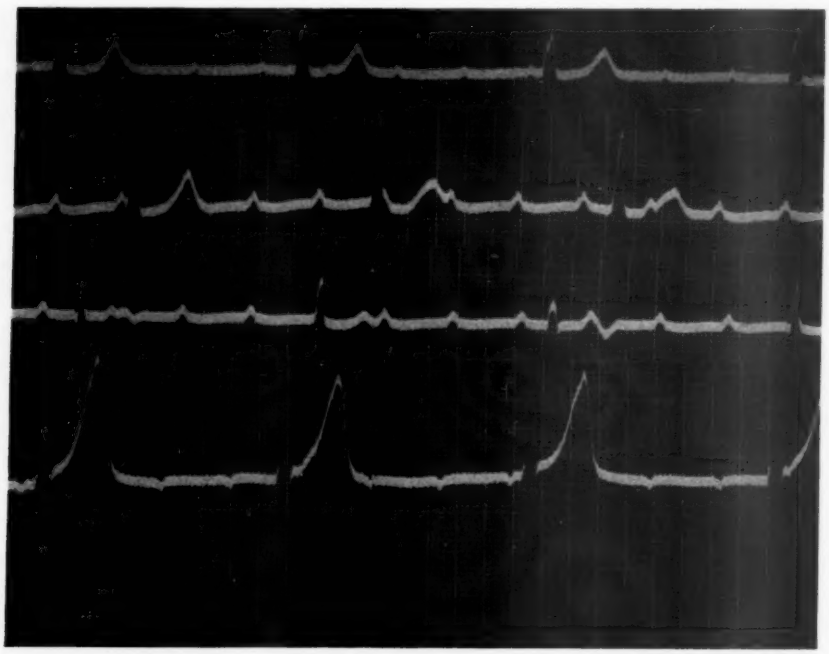
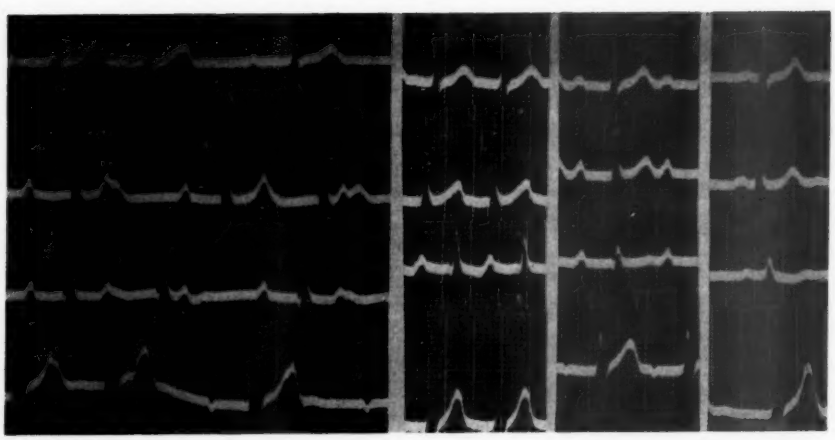


Fig. 1.



A. *B.* *C.* *D.*

Fig. 2.

2,800 white blood cells with 52 per cent polymorphonuclears, 36 per cent lymphocytes, and 12 per cent monocytes. At no time were atypical lymphocytes seen in the blood smears. The heterophile antibody test was repeatedly positive in titer increasing from 1:28 to 1:224. Approximately one month after the appearance of the eruption it was still positive in a dilution of 1:224. The sedimentation rate was 5 mm. in one hour. Preceding the eruption the temperature reached 102.5°. Following the appearance of the eruption, the temperature

rapidly returned to normal. The glandular swelling subsided during the next few days. Convalescence was uneventful, and after a furlough the patient returned to duty on June 8, 1943.

COMMENTS

The prolonged fever, cervical adenopathy, palpable spleen, papular eruption and positive heterophile antibody test warranted the consideration of acute infectious mononucleosis. The nature and extent of the generalized skin eruption, with sudden subsidence of symptoms following its appearance, and the absence of atypical lymphocytes made this condition seem unlikely. Consultants in dermatology and in infectious diseases felt that the eruption was typical of German measles. A hematology consultant felt that the blood picture was not that of acute infectious mononucleosis. Positive heterophile tests have been reported in pneumonia, scarlet fever, measles, tuberculosis, filariasis, and aplastic anemia.[6] The positive heterophile test in the present case was thought to be associated with the German measles.

SUMMARY

A case of complete heart block occurring during the pre-eruptive stage of German measles is reported. The heart block was of short duration, and at the end of two weeks the conduction time had returned to normal and the infection had subsided.

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Abstracts and Reviews

Selected Abstracts

Taquini, A. C., and Lozada, B.: The Ascending S-T Segment. Its Clinical Importance. Rev. argent. de cardiol. **11**: 231, 1944.

The perusal of two thousand clinical records of patients with various diseases showed that an ascending S-T segment was present in the electrocardiogram in seventy-seven cases. The presence of this electrocardiographic pattern, most frequent in D I and D II, had no relation to the type of thorax or to the position of the heart. It was more frequent in women than in men, and the diseases most commonly associated with it were the gall bladder diseases. An ascending S-T segment was also frequently found in climacterium and in intestinal disease associated with gall bladder diseases or along with it. AUTHORS.

Cabrera, E., and Pallares, S. D.: Determination of the Medium Manifest Axis of Unipolar Derivation of the Extremities. Arch. Inst. Cardiol. Mex. **14**: 135, 1945.

An improvement of Sodi's formula to obtain the direction of the manifest potential axis of a given electrocardiographic deflection by means of Wilson's unipolar limb leads is described. The authors give an algebraic method to obtain this formula.

A new method of trigonometric design similar to Einthoven's original one is described, employing the values of Wilson's unipolar limb leads, instead of those of Einthoven's standard limb leads. AUTHORS.

Pallares, S. D., Cuellar, A., and Cabrera, E.: Six Axis System With Application to the Vector AvT in Ventricular Hypertrophy. Arch. Inst. Cardiol. Mex. **14**: 142, 1945.

A six-axis system, which was inspired by Bayley's triaxial one and includes the three-axis system of Wilson's unipolar limb leads besides those of the equilateral triangle of Einthoven is presented. The manifest axis of the T wave in ventricular hypertrophies is related to this new system and several considerations are made in regard to the changes of this wave. AUTHORS.

Simonson, E., and Enzer, N.: An Unusual Case of A-V Nodal Rhythm With Varying A-V Block. Brit. Heart J. **7**: 45, 1945.

A case is presented with P-R intervals varying from plus 0.22 to minus 0.19 second. The type of P waves is nodal. Episodes of gradual shortening of P-R intervals, until P follows QRS, of blocked P waves followed by Wenckebach's phenomenon, and abrupt transition from R-P to P-R intervals were observed. Two alternative interpretations are offered: (1) assumption of nodal rhythm with varying degree of at least forward, and possibly of both forward and retrograde conduction, or (2) assumption of two nodal pacemakers.

AUTHORS.

Ashman, R., Ferguson, F. P., Gremillion, A. I., and Byer, E.: The Effect of Cycle-Length Changes Upon the Form and Amplitude of the T Deflection of the Electrocardiogram. Am. J. Physiol. **143**: 453, 1945.

In the normal heart, at ordinary heart rates, the observed T wave is mainly due to differences in the time required for repolarization of different muscle elements. Acceleration, or decrease of cycle length, reduces these differences and thus causes the associated changes which then occur in the form and amplitude of the T wave. AUTHORS.

Simonson, E., Enzer, N., and Goodman, J. S.: Coronary Insufficiency, Revealed by Ectopic, Nodal, and Ventricular Beats in the Presence of Left Bundle Branch Block. Am. J. M. Sc. 209: 349, 1945.

In a case of left bundle branch block, premature ventricular beats in Leads III and CF_2 in the first electrocardiogram and nodal escape beats in Leads CF_2 and CF_4 of the second electrocardiogram, taken one day later, revealed the presence of acute coronary ventricular block in the regular beats. There was an evolution of the inverted T waves in the ectopic beats of CF_2 from the first to the second electrocardiogram. Multiple ectopic beats, due to nodal escape, in the limb leads show a shortening of the QRS intervals to normal limits and a normal QRS contour. The possible mechanism is discussed. Since the mechanism producing the ectopic beats varied, it can be concluded that the pattern of myocardial infarct or coronary insufficiency may be revealed in ectopic beats in the presence of intraventricular block, to a certain degree independent of the mechanism producing the ectopic beats.

AUTHORS.

Mehta, J. B., and Hewlett, R. F. L.: Cor Triloculare Biauriculare. Brit. Heart J. 7: 41, 1945.

An account has been given of the heart from a woman who lived to be 56 years of age. It was a biauricular trilocular heart, but with an imperfect auricular septum. There was a single aorta arising from the ventricle. AUTHORS.

Robbins, S. L.: Brain Abscess Associated With Congenital Heart Disease. Arch. Int. Med. 75: 279, 1945.

Three cases of brain abscess associated with septal defects of the heart which came to autopsy at the Mallory Institute of Pathology of the Boston City Hospital during the years 1936 to 1943 form the body of this paper. The cases were selected from the 7,880 autopsies performed during these years, which included 53 cases of congenital heart disease of all types. There were no other instances of encephalomalacia encountered in the latter group. The total number of such cases in the literature to date is twenty-six.

In only three cases in the literature has an ante-mortem diagnosis of the disease been made and surgical drainage been instituted, a proportion which reflects principally the difficulty in diagnosis, arising in most instances from unfamiliarity with this complication of septal defects of the heart.

With the increased number of cases reported, it is to be hoped that in patients with congenital heart disease, especially in those having the tetralogy of Fallot, underlying brain abscess will be considered in the diagnosis of any focal neurological damage or meningitis. Certainly only early recognition will permit successful surgical intervention and hope for cure of this uncommon syndrome. AUTHOR.

Taussig, H. B.: Clinical and Pathological Findings in Aortic Atresia or Marked Hypoplasia of the Aorta at Its Base. Bull. Johns Hopkins Hosp. 76: 75, 1945.

Aortic atresia or marked hypoplasia of the aorta at its base causes the right ventricle to pump the blood not only to the lungs but also through the ductus arteriosus to the systemic circulation. This mechanism places a great strain on the right side of the heart and is extremely inefficient for the maintenance of an adequate circulation to the body.

The outstanding clinical features produced by this malformation are intense cyanosis, great right-sided cardiac enlargement, a weak pulse in both the arms and the legs, and a low blood pressure. Fluoroscopic examination shows cardiac enlargement due to the enormous enlargement of the right ventricle; the pulmonary conus of the right ventricle and the pulmonary artery proximal to the ductus arteriosus occupy their normal position but are markedly distended. Usually there is also distention of the right auricle and the superior vena cava. The electrocardiogram shows a right axis deviation. Cardiac failure occurs early. The condition is not compatible with life for more than a few days. AUTHOR.

Sisson, J. H., Murphy, G. E., and Newman, E. V.: Congenital Arteriovenous Aneurysms. Bull. Johns Hopkins Hosp. 76: 93, 1945.

A case of multiple congenital arteriovenous aneurysms in the pulmonary circulation is presented. The diagnosis established by angiography was confirmed at autopsy, and the

pathologic findings are reported. The clinical picture of six reported cases is summarized. The usual symptoms are weakness, faintness and dizziness, dyspnea, chest pain, and hemoptysis. The signs are cyanosis, clubbing of the fingers, often visible hemangiomata, bruit over chest, polycythemia, and x-ray evidence of a localized opacity in the lung. The diagnosis can be definitely established by angiography. The treatment is pneumonectomy.

A brief discussion is given of angiographic technique and the physiologic effects of pulmonary arteriovenous communications. Angiography has proved a useful procedure but may be dangerous in a patient with a circulatory shunt from right to left heart.

A clinicopathologic analysis is made of twelve previously reported cases together with the one reported of death following within one hour the intravenous injection of diodrast in diagnostic procedures. A possible conclusion one may reach from the breakdown of these data is that the intravenous use of diodrast should be approached with caution in the case of patients with hypertensive cardiorenal disease. AUTHORS.

Holyoke, J. B.: Coronary Arteriosclerosis and Myocardial Infarction as Studied by an Injection Technic. Arch. Path. 39: 268, 1945.

An unselected series of seventy adult hearts were studied by the Schlesinger injection technique.

Occlusions of the coronary arteries were demonstrated in twelve of the seventy hearts. In these twelve hearts, thirty-one points of obstruction were demonstrated. Thirteen were in the main stems of the three principal coronary arteries. Eighteen were in the large branches.

Interarterial anastomoses were demonstrated in all hearts with pronounced arteriosclerotic narrowing. Only in the presence of marked hypertrophy were such anastomoses demonstrated in other hearts.

In three of eleven hearts with old occlusions of the coronary arteries there were no old infarcts. In two of five hearts with recent occlusions of the coronary arteries there were no corresponding recent infarcts.

In one of four hearts with recent infarcts there was no recent occlusion.

Grossly recognizable scars were present in the myocardium of twenty-six of the seventy hearts.

Data from this work and from the literature emphasized that coronary arteriosclerosis is only one of the many factors which may be responsible for the anatomic changes and the symptoms resulting from myocardial anoxia. AUTHOR.

Johnson, R. S., and Lewes, D.: Advanced Mitral Stenosis at Three Years Old. Brit. Heart J. 7: 52, 1945.

A case of chronic (healed) rheumatic endocarditis with advanced mitral stenosis in an infant, aged 2 years and 10 months, is reported, together with the autopsy findings. AUTHORS.

Wilson, K. S., and Alexander, H. L.: The Relation of Periarteritis Nodosa to Bronchial Asthma and Other Forms of Human Hypersensitiveness. J. Lab. & Clin. Med. 30: 195, 1945.

In three hundred consecutive cases of periarteritis nodosa, bronchial asthma was identified in fifty-four, or 18 per cent. When differential blood counts were available, all but three of forty-seven cases of asthma (94 per cent) showed a hypereosinophilia ranging from 11 to 84 per cent, with an average of 53.5 per cent. This is in marked contrast to one hundred and fifty-one cases without asthma in which there were but nine instances of hypereosinophilia (6 per cent), and the average eosinophile count was 2.5 per cent. The association of periarteritis nodosa to the various forms of human hypersensitiveness is discussed. AUTHORS.

Duncan, G. W.: Venous Pressure as an Index of Blood Flow in the Upper Extremity. Arch. Surg. 49: 235, 1944.

In the experiments described, the measurement of the rate of rise in venous pressure in the large veins of the forearm following venous occlusion is, at least to some extent, an index of the rate of blood flow in the extremity. Local application of heat to the hand and forearm and exercise of the muscles of the hand and forearm increase the rapidity of rise in venous pressure, while local application of cold decreases it. AUTHOR.

Taquini, A. C., and Suarez, J. R. E.: Modification of Respiration and Circulation in Arteriovenous Aneurysm. Medicina, Buenos Aires 5: 109, 1945.

A report is made on five patients with arteriovenous communications; four were traumatic fistulas, three at the level of the femoral vessels, and one at the level of the deep femoral vessels. The other was a cirsoid aneurysm of the leg.

The pulmonary ventilation was increased with a diminished concentration of carbon dioxide in the expired air; the carbon dioxide tension in alveolar air, the vital capacity, and residual air were within normal figures in the patients who were investigated.

The minute cardiac volume was abnormally increased in three out of five individuals, with a diminished arteriovenous oxygen difference. In three instances, the venous pressure was determined and proved normal.

The total blood volume was remarkably increased in the three patients with an increased minute volume. The globular-plasmatic relationship was normal.

These observations were repeated in three individuals after pressure by hand on the femoral artery; in two cases there was a fall in the heart rate. The minute volume was the same as prior to the compression. The venous pressure increased in all three. AUTHORS.

Herbut, P. A., and Price, A. H.: Periarteritis Nodosa Producing Aneurysm of the Renal Artery and Hypertension. Arch. Path. 39: 274, 1945.

In a case of periarteritis nodosa of the renal arteries there was an old periarteritic renal aneurysm which produced narrowing of the vascular lumen, with renal ischemia, hypertension, and death from cerebral hemorrhage following. In a second case, multiple acute periarteritic aneurysms of the intrarenal branches of both renal arteries produced hypertension, with death resulting from rupture of one of the aneurysms.

The sequence of events in the first case indicates that an aneurysm of an extrinsic portion of a renal artery can produce hypertension provided the lumen of the vessel is occluded to a degree great enough to produce renal ischemia. AUTHORS.

Katz, L. N., Wise, W., and Jochim, K.: The Dynamics of the Isolated Heart and Heart-Lung Preparations of the Dog. Am. J. Physiol. 143: 463, 1945.

Two preparations, an isolated heart and a closed circuit heart-lung, are described in which the dynamics of the circulation could be analyzed under controlled conditions. The main differences between the two preparations are (1) that in the isolated heart preparation the circuit is interrupted between the pulmonary artery and left auricle by an artificial "lung" and a pump for returning blood to a reservoir, while in the heart-lung preparation the lungs are left in situ (the artificial "lung," pump, artificial pulmonary peripheral resistance, and reservoir being omitted), (2) that artificial control is obtained in the isolated heart preparation by varying the artificial peripheral resistance placed in both the pulmonary and systemic circuits and/or the reservoir height, while in the heart-lung preparation artificial control is obtained by varying the artificial peripheral resistance placed only in the systemic circuit and/or the amount of blood in circulation.

A total of seventy-nine experiments was analyzed, 44 isolated heart, and 35 heart-lung, preparations. Graphs of various measurements were made of all these experiments using the initial control levels. These were subjected to statistical analysis in order to gain information about the circulatory dynamics in these preparations and to further knowledge of the cardiodynamics in the intact circulation. Considerations of the control of coronary flow are deferred to a later report.

In general, the experiments were of longer duration; progressive heart failure was longer, delayed, and less brusque in its development in the heart-lung than the isolated heart preparations. Among the heart-lung preparations those in which heparinized blood was used survived longer than those with defibrinated blood. The presence of progressive heart failure in some of these preparations when the initial readings were made did not affect the graphs here analyzed in any significant manner.

The significance of the various findings on the interrelation of the variables analyzed is discussed briefly.

The outstanding fact observed was the greater degree of interdependence of the various pressures and flows in the heart-lung preparation compared to the isolated heart. This is attributed to the fact that in the heart-lung preparation the main change made is in the amount of circulating blood which tends to affect all the pressures and cardiac output at the

same time and in the same direction. The greater freedom of experimental adjustment in the isolated heart nullified this to a large extent. In the intact circulation, it would appear that the changes would be interrelated somewhat as in the heart-lung preparation insofar as the adjustments are due to alterations in circulating blood volume. Change in circulating blood volume is one of the most important, but not the only, means of adjusting the dynamics of circulation in the intact animal. However, the operation of compensaory mechanisms in the intact animal, chiefly of neurogenic origin, would modify the interdependence found in the isolated heart-lung preparation. AUTHORS.

Smith, J. R., and Henry, M. J.: Demonstration of the Coronary Arterial System With Neoprene Latex. J. Lab. & Clin. Med. 30: 466, 1945.

A method is described whereby neoprene latex is infused into the coronary vessels of the dog heart. Corrosion specimens, employing concentrated hydrochloric acid, may be made which appear to preserve all details of the coronary arterial system lumina including the capillaries. The cardiac chambers may be filled with liquid latex and the whole organ suspended by a glass hook to support the vascular casting when the myocardium is digested away. The finished specimen is kept immersed in fluid so that the minute strands are separated and details of the coronary vascular system may be seen. AUTHORS.

Friedberg, L., and Katz, L. N.: Observations on Shock Following Bilateral Venous Occlusion of the Hind-Limbs of the Dog. Am. J. Physiol. 143: 589, 1945.

Bilateral venous occlusion of the hindlimb of the dog by means of ligation and lampblack injection leads to a consistently fatal and rapid shocklike state. Early fluid administration (sodium chloride or plasma), demonstrated to be effective in preventing this state in unilateral venous occlusion experiments, is without beneficial action in these animals. Likewise, application of a rigid cast to both hindlimbs and lower abdomen, in order to minimize fluid leakage into the injured area, is accompanied by slightly increased length of life but does not prevent the ultimate fatal result. This suggests that some other factor, perhaps a humoral "toxic" substance plays a role. The mechanisms and possible interpretation of these results are discussed. AUTHORS.

Zweifach, B. W., Abell, R. G., Chambers, R., and Clowes, G. H. A.: Role of the Decompensatory Reactions of Peripheral Blood Vessels in Tourniquet Shock. Surg., Gynec. & Obst. 80: 593, 1945.

The purpose of this investigation was to determine whether, in tourniquet shock, the second, decompensatory factor always appears subsequent to fluid loss or whether it may be regarded as a primary factor which normally follows, but may be independent of, fluid loss.

Experiments were performed on dogs, cats, and rabbits in which shock was produced under pentobarbital anesthesia by several different tourniquet procedures. The studies involved two methods. One consisted of continuous observations on specific physiologic reactions of the arteries, arterioles, precapillary sphincters, capillaries, collecting venules, and veins of the exteriorized omentum or mesentery. The other consisted of testing blood samples removed at intervals during the shock syndrome. The serum was injected intravenously into normal rats, and the effect on the arterioles and capillary vessels was noted in the exteriorized mesoappendix.

The initiating factor in the peripheral circulation is a reduction in rate and amount of blood flow. This occurs while the damaged limb is swelling and is associated with vasoconstriction and with hyperreactivity of the terminal vessels as observed in the mesentery and omentum.

When the syndrome is fatal two sets of contributory factors are detected: an increased viscosity of the blood, indicated by a rise in hematocrit, and the development of hyporeactivity of the terminal blood vessels. The hyporeactivity occurred while the peripheral flow was still good and resulted in pooling of blood in the capillaries and venules, thereby intensifying the reduction in the circulating blood volume. In many cases, hyporeactivity was the decisive factor in the syndrome.

Circulatory collapse in tourniquet shock is due to a reduction in blood volume caused by: (a) loss of fluid into injured limb and (b) sequestration of blood from the active circulation by pooling in the capillary bed and collecting venules. The latter is due to the development of a hyporeactive factor, which progressively interferes with the peripheral vascular compensatory mechanisms. AUTHORS.

Ricca, R. A., Fink, K., Katzin, L. I., and Warren, S. L.: Effect of Environmental Temperature on Experimental Traumatic Shock in Dogs. J. Clin. Investigation 24: 127, 1945.

In order to obtain a reproducible standardized shock experiment with the Blalock type of crusher, it is necessary to use overall pressure of 2,000 pounds for five hours on one complete upper thigh under nembutal anesthesia with the room temperature at 28° C. or above.

Any variation in these several stipulations may change the picture enough to prevent the onset of fatal shock. AUTHORS.

Ricca, R. A., Fink, K., Steadman, L. T., and Warren, S. L.: The Distribution of Body Fluids of Dogs in Traumatic Shock. J. Clin. Investigation 24: 140, 1945.

In traumatic shock, the fluid which extravasates into the traumatized extremity is mobilized from the rest of the tissues of the body. A portion of it is contributed by loss of circulating plasma.

The A-G ration, as determined chemically, is higher in the leg fluid from the traumatized area than that of the plasma in every case. Cell proteins apparently are liberated in the traumatized extremely, probably from ruptured muscle fibers.

The nonprotein nitrogen content of the fluid in the traumatized area is higher than that of the blood. The liberated cell proteins probably undergo breakdown into simpler nitrogenous products. The elevated blood nonprotein nitrogen during traumatic shock may, to some extent, be due to absorption of these products.

Alterations in electrolyte concentration of serum and tissues which occur during traumatic shock have been tabulated. AUTHORS.

Del Solar, A. V., Dussaillant, G. G., Brodsky, M. B., and Rodriguex, G. C.: Fatal Poisoning From Potassium Thiocyanate Used in Treatment of Hypertension. Arch. Int. Med. 75: 247, 1945.

Another case, the seventh thus far reported, of death due to the therapeutic use of potassium thiocyanate for hypertension is added to the literature. A distinct fault in dosage on the part of the patient was responsible for the intoxication; it emphasizes the danger of prescribing the drug in easily inaccurately measured forms, like the solution for drop administration used for this case.

The thiocyanate concentration of the blood at the onset of toxic symptoms was only 7 mg. per hundred cubic centimeters. The concentrations of the drug in the tissue are the highest ones thus far reported in similar instances. A prominent feature of the post-mortem examination was the finding of an acute necrotic nephrosis that had produced no symptoms or signs during life. AUTHORS.

Hines, L. E., and Kessler, D. L.: Venesection for the Plethoric Patient. Arch. Int. Med. 75: 250, 1945.

Only two of fifty-eight patients proved to have had coronary thrombosis had an erythrocyte count of less than 4,000,000. Diminished clotting time after administration of heparin and a shortened prothrombin time were the common findings for patients with high erythrocyte counts.

Similar changes in the clotting mechanism have been observed in patients known to have thrombosis. These facts suggest that the use of venesection both for preventing and for treating thrombosis is rational. The changes produced by bleeding a small number of patients seem to support the idea. AUTHORS.

Books Received

PUBLICACIONES DEL CENTRO DE INVESTIGACIONES TISIOLOGICAS. Director: Professor Roque A. Izzo. Pabellon "Las Provincias," Buenos Aires, 1944, vol. VIII.

American Heart Association, Inc.

1790 Broadway at 58th Street, New York, N. Y.

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